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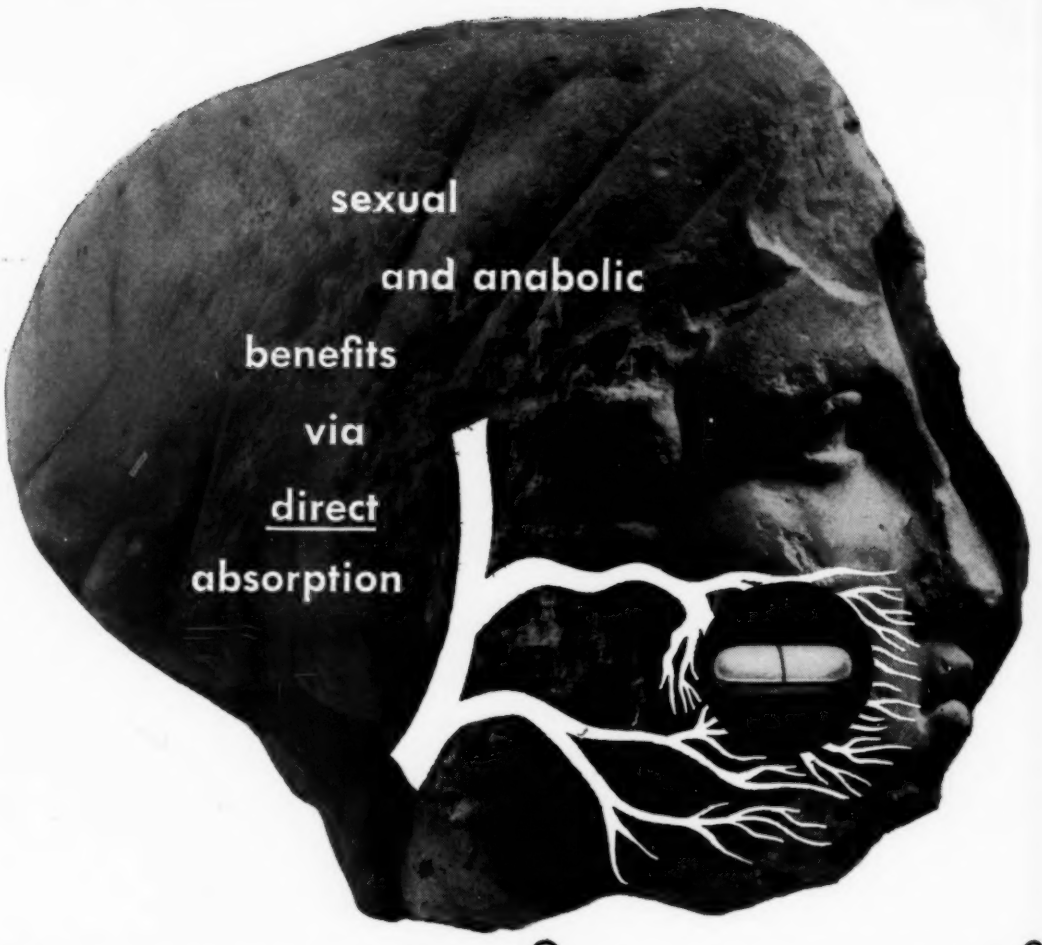


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JOURNAL OF

# The American Geriatrics Society

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VOLUME III *February, 1955* NUMBER 2

## ADRENOCORTICAL CAPACITY AND THE METABOLISM OF CORTISOL IN ELDERLY PATIENTS*

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Some years ago it was demonstrated that in elderly patients urinary 17-ketosteroid excretion is much less than in young adults. Albright (1) postulated from these and certain other data that an "adrenopause" occurs with aging, in much the same fashion that ovarian and, less frequently, testicular functions decrease. However, he suggested that this applied only to the androgenic (N) hormones secreted by the adrenal cortex. Although quantitatively and qualitatively cortisol (hydrocortisone) appears to be of major importance among the steroids secreted by the human adrenal cortex, it has very little androgenic potency and 17-ketosteroid excretion is a poor means by which to evaluate the secretion of this substance (2). With the development of a method for the measurement of 17-hydroxycorticosteroids in plasma (primarily cortisol) it has been possible to develop a number of techniques for evaluation of the metabolism of this steroid. We have applied these techniques in geriatric patients. The results show certain differences from those obtained in young adults and suggest that cortisol metabolism is modified in these patients, although the adrenal retains its ability to secrete this vital substance.

### METHODS

Patients were selected from the Infirmary of the Salt Lake General Hospital. Those with acute illness were excluded, as well as those with endocrine disorders and inflammatory disease. Their ages varied from 66 to 92 but they were active individuals. Blood for determination of plasma 17-hydroxycorticosteroids was drawn from a peripheral vein. Heparin was used as an anticoagulant and the cells were promptly separated from the plasma, which was stored in a refrigerator until analyzed. Determinations were carried out by the modification of the Nelson and Samuels method described by Eik-Nes *et al.* (3, 4). It should be noted that this technique determines all of the free 17,21-dihydroxy,20-ketosteroids

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in plasma. Although cortisone, cortisol, Reichstein's substance S and their hydrogenated derivatives give this reaction, nearly all of the free material in human plasma appears to be cortisol (5). Methods previously described were used for the evaluation of adrenocortical capacity and rate of disappearance of exogenous cortisol (6, 7).

## RESULTS

### *Plasma levels of 17-hydrocorticosteroids under basal conditions*

The mean level of 17-hydroxycorticosteroids and its standard error in 16 patients in the basal state at 9:00 a.m. was 15.6 ± 1.2 μg./100 ml. of plasma. In a larger series of young adults, the level at this time was 13.2 ± 0.9 μg./100 ml. of plasma. Statistical evaluation of this difference showed that the probability of its occurrence by chance alone was 11 in 100 times. The significance of the difference is therefore uncertain.

### *Adrenocortical capacity*

In Table 1 the effect of a six-hour ACTH infusion on the plasma 17-hydroxycorticosteroid levels of 5 elderly patients is presented. In Figure 1 the average of these data is compared with the average observed in a larger series of young adults. Although the character of the curves is similar, the levels attained in

TABLE 1

*Adrenocortical Capacity in Geriatric Patients*

| Age | Plasma 17-hydroxycorticosteroid levels (μg./100 ml.) | | | |
|---|---|---|---|---|
| | Control | 2 hrs. | 4 hrs. | 6 hrs. |
| 78 | 15 | 65 | 58 | 67 |
| 81 | 18 | 47 | 57 | 66 |
| 92 | 16 | 37 | 52 | 64 |
| 83 | 15 | 59 | 64 | 60 |
| 81 | 16 | 50 | 65 | 70 |
| *Mean* | *16* | *51.6* | *59.2* | *65.4* |

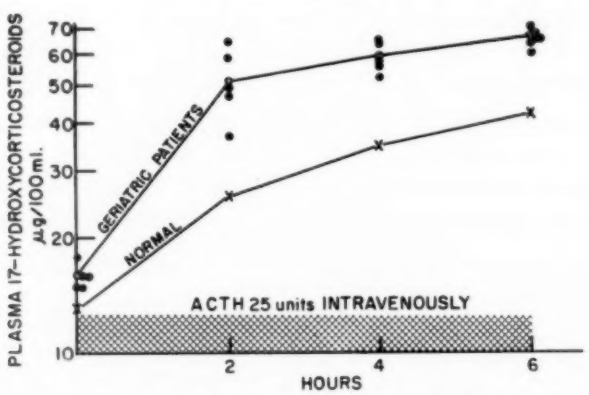


FIG. 1. The effect of a continuous six-hour infusion of ACTH on the plasma levels of 17-hydroxycorticosteroids in normal young adults and in geriatric patients.

TABLE 2

*Cortisol Degradation in Geriatric Patients*

| Subject | Age | Plasma 17-hydroxycorticosteroid levels (μg./100 ml.) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Control | 30 min. | 1 hr. | 2 hrs. | 4 hrs. | 6 hrs. | 8 hrs. |
| 1 | 79 | 6 | 225 | 154 | 104 | 60 | 47 | 29 |
| 2 | 72 | 15 | 264 | 163 | 124 | 70 | 50 | 42 |
| 3 | 75 | 20 | 206 | 148 | 90 | 39 | 27 | 15 |
| 4 | 72 | 10 | 147 | 122 | 80 | 76 | 28 | 17 |
| 5 | 83 | 23 | — | 168 | 108 | 37 | 26 | 18 |
| 6 | 77 | 11 | — | 184 | 162 | 79 | 41 | 33 |
| 7 | 72 | 18 | — | 166 | 149 | 77 | 60 | 20 |
| 8 | 66 | 10 | — | 162 | 86 | 50 | 33 | 43 |
| 9 | 80 | 20 | 106 | 90 | 49 | 36 | 23 | 16 |
| 10 | 84 | 11 | 199 | 162 | 105 | 63 | 54 | 27 |
| 11 | 68 | 26 | — | 165 | 70 | 30 | 25 | 9 |
| *Mean* | *75.3* | *15.5* | *191* | *153* | *102.5* | *56* | *38.6* | *24.5* |

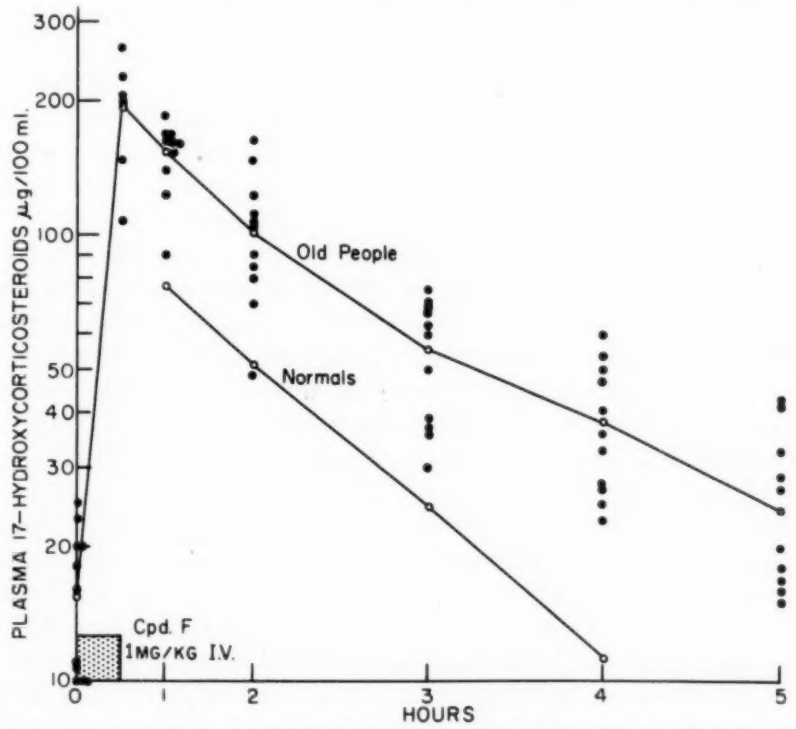


FIG. 2. Rate of removal of cortisol (hydrocortisone) from the plasma in young adults and in geriatric patients after the infusion of 1 mg. per kilogram of body weight over a half-hour period.

the geriatric patients were significantly higher than those observed in younger subjects.

*Disappearance of exogenous cortisol*

The data obtained in geriatric patients after the infusion of 1 mg. of cortisol per kilogram of body weight is presented in Table 2. In Figure 2 the mean result

is compared with that obtained in young adults. Again it is obvious that higher plasma levels developed in the elderly patients than in the younger subjects. However, the proportion of cortisol removed from the plasma per unit of time was essentially identical during the first hours. In the geriatric patients the level had fallen to half of its initial level in 100 minutes, whereas the value was 95 minutes in the young subjects. Subsequently the two curves are not parallel, because the rate in the elderly patients lagged behind that in the controls. Between the fourth and eighth hour the "half life" had increased to 215 minutes in the geriatric patients. It is difficult to compare values in this period with those in the control subjects because their curve appeared to continue at the same rate up to the sixth hour, when the value had fallen into the normal range. Thus this late change in the rate of removal of steroid by the geriatric patients could be due either to a difference in its catabolism or to an effect of the higher initial level which the infusion produced.

## DISCUSSION

This evidence would seem to establish clearly that there was no gross deficiency in the secretion or metabolism of 17-hydroxycorticosteroids in these elderly patients. On the other hand the levels produced by ACTH and steroid infusion were higher in the geriatric patients than those observed in younger subjects. On first inspection of the control levels and ACTH response one might be tempted to speculate that the adrenals of elderly patients were capable of a greater secretion rate. However the fact that comparable infusions of cortisol also produced higher levels in the geriatric patients makes this hypothesis untenable. It might be supposed that hepatic blood flow and function were impaired in these elderly individuals. However the data are at variance with those of Brown *et al.* (7) in patients with hepatitis and cirrhosis, using these same methods. Most critically, the fact that the initial rate of removal from the plasma was the same in the normal individuals and the geriatric patients, in contrast to the delayed removal observed in patients with impaired liver function, would seem to eliminate this possibility also.

Therefore it seems improbable that either the secretory rate or the removal rate, primarily a hepatic function, was seriously abnormal in the geriatric patients. In the light of these conclusions it seems probable that the differences were the result of modified distribution between the plasma and other body fluids and tissues. Such a hypothesis would explain the greater rise in the plasma 17-hydroxycorticosteroid level after ACTH, as well as the higher initial level with a normal removal rate after cortisol infusion.

The reason for such a difference in distribution between young and old is not apparent. If the initial volume of distribution is estimated by extending the logarithmic curves back to zero time (Fig. 2), we find that it is approximately half as great in the elderly patients. These estimates are inaccurate (because the infusions were carried out over a 30-minute period) but none the less comparable for the two groups. Determination of 17-hydroxycorticosteroid levels in normal and abnormal body fluids has shown that they are in general less than simul-

taneous plasma levels (8). No data are available from which the intracellular concentration of steroid can be estimated. However, on theoretical grounds, we might expect to find these fat-soluble materials initially concentrated in fatty tissues. Actually elderly patients tend to have a lower proportion of subcutaneous fat and such an explanation seems reasonable as a hypothesis to explain the observed difference in distribution. However, if this were the mechanism, it would be expected that the one-hour levels should show a good gross correlation with the relative obesity or thinness of the individual patients. Actually a number of striking exceptions to this rule were observed. For example, Patient # 1 weighed only 109 pounds and was nearly 6 feet tall, yet had one of the lower plasma levels. On the other hand, Patient # 7 who weighed 194 pounds and was approximately the same height, had a higher level.

The data on a number of the other patients would fit such a hypothesis. For example, Patient # 9 who weighed 167 pounds but was 68 inches tall, had a degradation curve which was not significantly different from the data on normal young adults. However, all of the other values are consistently higher than the normal by more than two standard deviations and form a consistent group without regard to relative obesity. Thus the possibility of preferential distribution to body fat is not confirmed by this type of analysis of the data. It is also well established that the extracellular fluid volume is somewhat smaller in elderly patients. However, the very large difference in apparent distribution volume would seem to argue against this as the only factor in the observed changes. The problem of the nature of the difference in distribution of cortisol between geriatric patients and young adults remains not entirely explained at present.

In spite of these problems in the interpretation of the physiologic significance of the data, certain presumptive conclusions about the use of ACTH and cortisone in the treatment of geriatric patients are indicated. Because of the higher plasma levels attained, it would be expected that comparable doses of these substances would produce greater metabolic effects in such patients, and that somewhat smaller doses would prove to be equally effective therapeutically. On the other hand the apparently smaller distribution volume could be interpreted as evidence of a smaller amount of the hormone reaching the peripheral cell, which is undoubtedly the final site of action of the hormone. Although the latter possibly seems less reasonable, decisions regarding dosage of hormones must be made on the basis of metabolic and therapeutic effects produced in the individual patient. The malignancy of the clinical disease and its presumed susceptibility to modification by the induction of hypercorticism are considerations equally as important as the degree of hypercorticism induced.

## SUMMARY

1. Geriatric patients had higher morning plasma levels of 17-hydroxycorticosteroid than did young adults, although the difference was not significant statistically.

2. After ACTH infusion, their plasma levels rose significantly higher than those observed in younger controls.

3. Following cortisol (hydrocortisone) infusion the levels were also higher, although the rate of removal from the plasma was similar during the first hours.

4. These data are interpreted as evidence that adrenal 17-hydroxycorticosteroid secretion and metabolism are relatively unmodified in the elderly, but that the volume of distribution of the steroid is smaller.

5. Certain therapeutic implications of the data are discussed.

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# SURGICAL EXPERIENCE IN THE AGED AS AN AID TO SURGERY IN THE YOUNG*

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Most discussions on surgery of the aged deal first with the increasing incidence of, and need for operation in older patients, and second, with the reduced mortality now experienced in this group. As an example of the latter, at the Barnes Hospital during a one-year period (1953–54), 714 surgical procedures were carried out in patients aged 70 to 96; death occurred in 27—a mortality rate of 5.5 per cent. There was a similar mortality rate in 239 procedures listed as general surgery; 12 patients died. However, on breaking down these figures into elective procedures, it was found that in 107 cases the following operations were carried out: hernia in 28, gastrectomy in 13, amputation in 18, sigmoid resection in 10, radical mastectomy in 15, and cholecystectomy in 13. There was only 1 death—in a patient operated upon for gallbladder disease but in whom extensive carcinoma was found.

The present communication deals with an inquiry into the causes for the reduced mortality in geriatric surgery during the past decade or two and how this knowledge has been applied to surgery in the younger patient. For convenience, these advances in surgical therapy may be partly classified into six arbitrary groups.

## I. VALUE OF BODY MOVEMENT AND OF EARLY AMBULATION

As a surgical resident I operated upon a 90-year-old man with a strangulated inguinal hernia and remember the unqualified admonition by the visiting surgeon as to the urgent necessity of getting the patient out of bed into a wheel chair as soon as he was awake from the anesthesia. The reason was: "old individuals do not tolerate bed rest." This was about twenty-five years ago. Since then the potential dangers of bed rest have been emphasized by many observers, not only in surgical patients but in medical patients as well, and in individuals of all age groups. It is curious that early ambulation, considered essential for the older surgical patient, was apparently too drastic for the younger one. Actually its value was so evident in the older group that few failed to recognize its importance. Nevertheless, we owe the benefit of body movement and early ambulation in the young to the fact that it was so dramatically demonstrated in the older age group.

## II. IMPORTANCE OF METICULOUS "MINIMUM" ANESTHESIA

Some years ago certain surgeons boasted that their patients had been so well anesthetized that they did not awaken until twenty-four hours after operation

* Presented at the Annual Meeting of the American Geriatrics Society, San Francisco, California, June 17–19, 1954.

and thus were spared all of the immediate postoperative discomfort. Many surgeons still demand such deep anesthesia during an abdominal operation as to produce almost "cadaveric" relaxation. However, in the aged, it was not the custom to use such deep or prolonged anesthesia because it was followed by a high mortality. It was thought, therefore, to be suitable only in younger patients. It soon became recognized that since all anesthetic agents are toxic, the best type of anesthesia is one which uses the smallest dose of drug. The more extensive use of the local or regional type carries out this principle, even when general anesthesia is also used. For example, in a series of older patients treated with nailing of intertrochanteric fractures at the Homer G. Phillips Hospital, as reported by Robey (1), infiltration of the fracture site with Novocaine as part of the preoperative preparation was found to reduce considerably the amount of general anesthetic agent necessary, and thus reduce the hazard of the procedure. As soon as the idea of "minimum" anesthesia was accepted and applied, the reduced mortality and incidence of complications were first readily apparent in the older age group. This lesson was then applied to all patients, so that better anesthesia is now the rule rather than the exception. Here too, principles learned in the old are now used in the young.

This same experience can be cited in the use of drugs for analgesia or sedation. There are probably few practitioners who do not realize the potential danger of depressant drugs in the older individual. The barbiturates are a common example. I encountered this well known fact many years ago and as a result began using sedatives which are not so harmful, *e.g.*, chloral hydrate and paraldehyde. I now use barbiturates less and less, even in younger patients. Actual bedside experience has taught me that chloral hydrate can be given in doses sufficiently large to produce sleep without any untoward depressant effect. In contrast, barbiturates, in sufficiently large dosage to achieve the same effect, are definitely depressant. When the oral route cannot be employed for administration of choral hydrate, the rectal route is satisfactory.

Another common example is in the use of morphine and its derivatives, which in the usual dosages may be hazardous in the older patient because of the depressant action. In such a case, a much smaller dose is usually selected or, still better, a combination of codeine and sodium luminal (30 mg. and 60 mg., respectively); this will often achieve the same effect without any respiratory or cerebral depression. So effective is this combination that I have learned to prefer it to morphine, even in younger patients.

### III. DANGER OF EXCESSIVE ADMINISTRATION OF PARENTERAL FLUIDS

It was natural, when the great benefits of correcting water and electrolyte deficiencies were first observed many decades ago, that this method of therapy would be used extensively. It is still a dramatic experience to see a patient severely dehydrated from excessive vomiting or diarrhea literally awakened from his stupor by the infusion of salt solution. Moreover, decades ago there was a great reduction in the high mortality following operation for intestinal obstruction or pyloric stenosis (then supposedly due to a toxemia) as soon as water and

electrolyte deficiency was corrected by preoperative preparation with parenteral fluids. It was not immediately recognized, however, that this therapy can not be used heedlessly. It is effective and life-saving only up to the point of correcting deficits; beyond this point, additional infusions impose upon the body a problem of excretion which may not be met adequately. Moreover, the deficits are so varied that one needs to know not only how much water to give, but also what electrolytes to add and in what concentration. Despite the existence of adequate knowledge in this field, one sees current examples of the injection of excessive amounts of water and/or of electrolytes, particularly at the two extremes of life—infancy and old age.

Excessive water and electrolyte loads can usually be handled by the younger unanesthetized adult. This ability is greatly reduced under the influence of anesthesia and operation. It is further reduced if the patient to be operated upon is in the older age group. The aged patient cannot handle such loads, presumably because 1) his kidneys are not as efficient as are those of the younger individual, 2) his capillary permeability is greater, and 3) he suffers from protein deficiency. In any case, the danger of tissue and pulmonary edema is so great that one must meticulously avoid the injection of more water and salt than is actually needed. A detailed experience was reported several years ago by Dr. Sid Ziffren of Iowa City; about 1947 he systematically combated the frequent tendency toward the infusion of excessive parenteral fluids following operation in the older age group, and was able to demonstrate a gratifying decrease in overall mortality.

Occasionally the over-zealous use of water alone, or failure to add sufficient salt to the water when both are needed, leads to water intoxication. The clinical picture is readily confused with a cerebral vascular accident—a condition which, in the aged patient, is apt to be passed up without diagnostic confirmation or corrective therapy. Water intoxication is prone to occur following transurethral resection in the aged, particularly when the patient has been on a salt-free diet because of cardiac disease. The mechanism is related apparently to the use of electrolyte-free fluids during the irrigation procedure.

Blood transfusions must also be mentioned in connection with parenteral fluid administration, although excessive blood transfusions are perhaps fairly uncommon in older patients because of the general fear of "overloading the circulation." However, younger individuals are frequently over-transfused and pulmonary edema develops. Even though the patients recover from the edema, its occurrence shows that the lesson has still not been learned adequately.

### IV. IMPORTANCE OF PREOPERATIVE NUTRITIONAL PREPARATION

The knowledge regarding water and electrolyte deficits as a preoperative handicap needs only to be carried to the other nutritional elements, particularly protein and vitamins, to realize the importance of nutritional preparation for operation. What have we learned from the older patient in this field? The evidence is hard to document, but it is the clinical impression of many observers that older patients respond better to operative procedures which are carried out only

after serious deficiencies in vitamins and protein have been corrected. This point of view has been well discussed in the paper by Dr. Cole, given in this symposium.[1] It is known that adipose tissue tends to form a larger proportion of the body weight in the older patient than in the younger, which in itself may not be so significant except that it is often associated with tissue protein deficiencies. A high protein diet in such cases is definitely indicated, but the length of time required to correct tissue protein deficiencies must be weighed carefully against the disadvantage of delay in carrying out needed surgical procedures. The oral route can be used in practically all patients, even though one may have to resort to special devices such as liquid diet or tube feeding.

Deficits in plasma protein and hemoglobin are easier to correct. The value of blood transfusions in nutritional preparation is obvious in the presence of anemia or hypoproteinemia, particularly if there has been evidence of blood loss. The hazard of operating upon a patient with a low hemoglobin level has long been recognized by anesthetists, especially in the older age group, and is now being equally recognized by surgeons with regard to patients at all ages, including infants and children. In the presence of anemia, the amount of blood needed is easy to determine, *i.e.*, sufficient should be given to restore the hemoglobin to a normal level. However, blood transfusions may also be valuable in the severely malnourished individual, even though the plasma protein and hemoglobin concentrations are normal. In the past, such preoperative transfusions have been withheld in the older age group for reasons already mentioned. A detailed report by Beling *et al.* (2) has offered convincing evidence of its value. They studied 100 elderly patients who were given an average of 1,500 ml. of blood before operation, based upon replacement of deficits as determined by blood volume studies; they compared these results with those in 190 similar patients given blood (average, 750 ml.), based merely upon the presence of anemia or upon bedside indications. The findings were rather striking. In the first group, the mortality was 8 per cent; in the second group, 17.4 per cent. Postoperative shock was absent in the first group but present in 3 patients of the second group. Most interesting was the incidence of cardiac failure—absent in the first group but present in 10 patients of the second group. This experience shows that adequate blood transfusion as preoperative preparation in the elderly patient is not only without danger, but probably has considerable value in terms of minimizing shock, mortality, and even the likelihood of cardiac failure. A study of preoperative blood transfusions was made by Nelson *et al.* (3), who used an average of 2 to 3 liters of blood, given at a rate of 500 to 1,000 ml. per day. They were impressed by the stability of the blood pressure and freedom from shock during and after operations in patients so prepared. Confirmatory evidence was reported by Ellison *et al.* (4), who felt that preoperative transfusions resulted in a reduction in mortality in many cases.

The principle is that when a deficiency exists in the circulating blood volume, replacement before operation is an effective form of preparation which may even reduce the need for blood transfusions during or after operation, thus illustrating

[1] *J. Am. Geriat. Soc.* **2**: 786 (Dec.) 1954

the old adage that an ounce of prevention is worth a pound of cure. Its application to the surgical therapy of the younger patient may be less evident but it is just as important.

### V. SYSTEMIC REACTION

The nonspecific systemic reaction to operation in the older patient is undoubtedly different from that in the younger individual. It is an old observation that, barring complications, the older individual has a relatively more benign postoperative course, presumably because he does not suffer as much apprehension, fear and tension as does the younger individual. If this be true, the surgeon should help the patient to achieve a relaxed, confident state of mind, regardless of his age. In any case, the feeling is becoming more general that psychogenic factors play an important part in preoperative and postoperative care of all patients, even though older patients seem to need it the least.

The relatively benign course so often shown by older patients during uncomplicated recovery has sometimes been explained by the supposition that they have a less intense adrenal-pituitary reaction as compared with the younger individual. This inference is drawn from certain observations which show that there is a lower excretion of adrenocortical hormones in the urine following operation in the aged. This is an intriguing idea, but requires more evidence before it can be accepted. We have been interested in studying the degree of the pituitary-adrenal reaction after operation, by measuring the blood levels of adrenocortical hormones before, during and afterward. Thus far, however, we have not been able to demonstrate any consistent differences between patients of various ages. Dobriner (5), in what is perhaps the most complete study of urinary adrenocortical hormones, found that at least in the resting state there is no difference between young and old individuals. A similar study after operation would be most informative.

### VI. MANAGEMENT OF MASSIVE GASTROINTESTINAL HEMORRHAGE

The surgical versus the medical treatment of massive upper gastrointestinal hemorrhage has been a topic of perennial interest for some time. With few dissents, most observers have presented evidence indicating that with a variety of nonoperative therapeutic procedures, the risk of gastrointestinal hemorrhage is greater with advancing age. The most recent data have been well documented by Pedersen of Copenhagen (6), who analyzed the results in several hundred patients treated by the method of Meulengracht, which includes prompt, frequent feedings and blood transfusions. Whether the transfusions were designed to replace the lost blood completely, or merely to combat shock, is not stated. However, the material between 1938 and 1948 was studied and, regardless of the method of analysis, an increasing mortality was observed with advancing age. Even if patients suffering uncomplicated exsanguination were selected, it was found that death occurred in 2 out of 21 (10 per cent) between the ages of 40 and 49; in 9 out of 33 (27 per cent) between the ages of 50 and 69; and in 3 out of 7 (43 per cent) in the age group above 70.

Evidence of a similar nature has been obtained from other parts of the world. For example, Blackford and Cole (7) in Seattle, Washington, found that 96 per cent of all deaths due to hemorrhage from peptic ulcer occurred in patients over the age of 45; yet careful studies from the Mason Clinic of the same city showed that the incidence of massive hemorrhage was just as high below the age of 45 as it was above. The increasing mortality with nonoperative therapy in the older age group was also reported by Køster (8), who found in carefully selected cases for comparable analysis that of 35 patients, 12 were operated upon; of these 2 died, aged 41 and 69. Of the 23 not operated upon, 3 died, aged 67, 73 and 73 (the first 2 from cardiac failure). Data from Greece were presented following the communication from Køster, citing similar experience, all of which showed that the mortality with nonoperative therapy was particularly great in patients above the age of 45. Thus these observers were led to abandon nonoperative therapy and to operate more promptly in the older age group.

Gordon-Taylor (9), though not mentioning the influence of age, distinctly showed the importance of early operation in patients with massive gastrointestinal hemorrhage. Of 18 patients operated upon within twenty-four hours of the hemorrhage, 1 died (a mortality of 5.5 per cent); whereas of 11 patients operated upon later, 4 died (a mortality of 36 per cent). This is an experience which we can duplicate even more strikingly from two hospitals in which the author works.

The reasons for this difference are probably similar to those already mentioned for other stresses, *i.e.*, that the older individual has a less efficient compensatory mechanism and therefore withstands many stresses less effectively than the younger person. Loss of blood produces not only circulatory impairment, but also an acute deficiency in plasma protein and hemoglobin concentrations, deficits which are tolerated less well by older than by younger patients. It was therefore clear that the program would have to be changed for the older patient if mortality was to be reduced. Thus it came about that operation was advised earlier rather than later in this group, based on the idea that elimination of the source of hemorrhage by operation was more important in the older patient. Finsterer (10) in 1939 was probably the first to recommend early operation in older patients with massive upper gastrointestinal hemorrhage, and a few recorded experiences seemed to show a gratifying reduction of mortality. In a report from England by Parsons and Aldridge (11) 50 cases of massive hemorrhage are described; all the patients were operated upon, and 7 died. Thirty of the 50 patients were under 50 years of age; of these, 5 died (a mortality of 17 per cent). Twenty patients were over the age of 50; of these only 2 died (a mortality of 10 per cent). These figures suggest that, unlike medical mortality, surgical mortality is not lower in the older age group. However, this is only one aspect of the problem.

When we first began our studies on massive gastrointestinal hemorrhage, we found a distressingly high mortality. Although it was greater in the older patient, many younger patients in their 30's or 40's died of exsanguination. Stimulated by the experience of John Stewart, who showed the value of early operation and of Costello, who showed the value of adequate blood replacement, we instituted

what we thought was a satisfactory program and observed a gratifying change in the mortality rate, both in the older and in the younger age group. Thus we learned that one set of principles should be applied to massive hemorrhage, regardless of the patient's age, even though the results were apt to be more striking in the older patient. Following such a program, we have had no deaths for three years. About half of the patients were operated upon as emergency cases, and half recovered with nonoperative therapy. The differentiation as to the need for operation was made on an individual basis, following a program based upon 1) emergency care, regardless of the hour, 2) adequate blood replacement, 3) frequent feeding. Operation was carried out promptly when there was an affirmative answer to either of two questions—is the hemorrhage continuing or has it recurred?

A corollary to the advantage of early surgery in massive gastrointestinal hemorrhage is the importance of prompt operation in other surgical emergencies. Formerly surgeons felt that, since operation was hazardous in the aged, it was better to avoid it, or to postpone it as long as possible. Most surgeons will now agree that a needed operation in the older age group should be performed early rather than late, because delay is more apt to be fatal in the old than in the young. This is clearly true in patients in whom operation will be eventually necessary. Examples are the hazards of prolonged expectant therapy for intestinal obstruction, or delay in the treatment of fractures. If one is reasonably sure that the procedure will eventually be needed, it should be carried out as early as possible. In this field, too, the experience in the older group has been applied with benefit to the younger patient. Procrastination and delay in needed surgical procedures should be avoided at all ages.

Data on intertrochanteric fractures were assembled by Robey at the Homer G. Phillips Hospital in St. Louis. Formerly only the young were subjected to operation and the older patients were treated "conservatively" for reasons already mentioned. However, the mortality was so high in the latter group that the tendency was reversed and now operation is preferred for the older group, and nonoperative therapy for the younger. This change in policy has been followed by a striking reduction in mortality. For example, there were 18 cases of intertrochanteric fracture in patients aged 70 to 101, during a period when operation was not performed promptly. Of these patients, 15 died (a mortality of 80 per cent). In a more recent period when all patients were operated upon early, there were 25 cases in this age group. Of these patients, only 9 died (a mortality of 38 per cent). A similar difference was observed in the number of complications. The incidence was 35 per cent in those operated upon, as compared with 80 per cent in those treated without operation. Thus the least hazardous therapy in the older group of patients with intertrochanteric fractures is prompt operation.

Still another example of the importance of prompt operation for obvious correction of surgical conditions is in the case of herniotomy. Failure to recommend operation in older patients is usually due to fear of a fatal outcome. However, when performed as an elective procedure, the risk is slight, but is increased when strangulation occurs. In a study by Strenger (12), 62 patients over 60 years of

age had elective herniotomies and only 1 died (a mortality of under 2 per cent); during the same period 20 patients had emergency operations for strangulation; of these, 8 died (a mortality of 40 per cent).

## SUMMARY

The present thesis may be stated briefly as follows: Surgeons have learned that the aged patient will successfully withstand even extensive surgical procedures with comparative safety, provided certain precautions are taken and certain mistakes avoided. These measures apply equally to the younger individual, even though without them he may do well and (unlike the aged patient) have relatively few complications, and a low mortality rate. Nevertheless, any improvement in surgical therapy should be applied to all individuals, regardless of age. The lessons learned in surgery of the aged are many and have now been applied to surgery of the young, with great benefit to both groups. A few of them have been discussed in detail.

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# PHYSIOLOGIC RESERVES IN THE AGED: APPLICATION TO OPERABILITY*

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An active, alert woman 90 years old once gave an intriguing answer to the question of longevity. She believed that at birth each of us is endowed with a specific number of tons of food and a specific number of hours of physical activity. When one has used up his predetermined allotment of either nourishment or activity, death takes over. One can go through these allotments rapidly and die early, or one can budget them carefully and live long. The eating habits and the physical activity of the elderly patient provide a "rough index" for determining operability. As the little woman of 90 would say—they indicate to us how much of the "allotted reserve" remains to the patient. The final determination of operability and the safety of the operation are proportional to the skill with which the surgeon can estimate, restore, support, protect and budget all the body reserves.

The aging process is essentially one of decreasing reserves. The importance and degree of this depletion vary in each of the organs involved. Aging consists of both physiologic and anatomic changes, which are complicated and modified by diseases, past and present and by habits of eating and physical activity (1, 2). Perhaps the most generalized physiologic change in the aged is decreased elasticity.

## DECREASED ELASTICITY

This alteration is based on the actual anatomic decrease in elastic fibers throughout the body. As a result the vascular system becomes less able to adjust to any changes—whether this change is due to increased demand from the surgical procedure, depletion from hemorrhage, or too rapid restoration of blood volume by the surgeon.

Chronic and generalized manifestations of this decreased elasticity of the vascular system are evident in the various organ systems. There is a relative inability to meet the changing daily and hourly nutrition requirements within the body. Coincidentally, or as a result, the active parenchymal cells in each organ decrease quantitatively and the interstitial supporting tissue increases.

### *Kidney*

The glomerular and tubular atrophy in the senile kidney is presumably a result of the foregoing process. There is a diminished ability of the kidney to concentrate, and therefore an increased need for available water to get rid of the waste products.

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The tubules are less able to conserve sodium. The senile kidney may continue to lose sodium, even though the body is in need of this element. This sodium loss is magnified by the decreased ability of the aging kidney to manufacture ammonia (a sodium-saving mechanism).

*Lungs*

In the lung, the decrease in elasticity results in emphysema, which interferes with the gaseous exchange of oxygen and carbon dioxide. This exchange may be adequate except under unusual stress. The elderly surgical patient has an increasing need for oxygen. Inability to get rid of all the carbon dioxide results in metabolic acidosis.

*Body fluids, electrolytes and proteins*

In the elderly, the relative frequency of a decreased blood volume enhances the inefficiency of the less elastic vascular system. Since in all age groups vascular content is directly dependent on the intercellular fluids and electrolytes, restoration of the blood volume is only a partial answer to restoration of the body fluids. The ease with which fluid is shifted from the intercellular spaces to meet any sudden demands of the circulation is decreased in the aged. Due to still unknown factors, the fluid reserves and compartments in an older individual can undergo sudden and complete depletion, even though, according to all tests, the quantity and quality are within normal limits.

As in the young, depletion of electrolytes parallels that of body fluids (1). Determining the amount of this deficiency, or the amount required for restoration to normal, is the same in the aged as in the young. However, the restoration must be at a more leisurely rate and carried out with greater care in the aged. Again, this is based on the principle that the elderly react more poorly to any sudden change.

Before restoring blood volume with plasma or plasma substitutes, adequate intercellular water and electrolytes must be made available by previously infused fluids (usually physiologic salt solution with 5 per cent glucose). In turn, before replenishing potassium, both intercellular and intravascular compartments should be restored. Until this is accomplished, renal excretion is inadequate and the infusion of potassium may result in dangerously high levels in the blood, even though the body is in need of this element.

## MISCELLANEOUS

*Nervous system: decreased sensitivity*

The anatomic degeneration and atrophy of the aging nervous system diminishes the normal response of the various organ systems to stimuli, both external and internal. Partly, as a manifestation of this, the pulse and febrile reactions of the elderly are less reliable clinical criteria than in younger persons. The internal temperature controls are less reactive; thus older patients are more sensitive to environmental temperature changes. Sweating is decreased; the in-

sensible water loss is half to two-thirds of that in the young. There is a relative indifference to food.

These factors plus many others lead to poor eating habits and, in turn, to inadequate protein stores, diminished body fluids and electrolytes, smaller blood volume and decreased vitamin levels. One should, in principle, presume that the elderly patient is deficient in these respects and that operability will be increased by replenishment of the depleted elements. If the elderly patient has lost weight, one can be certain that these reserves are diminished.

*Endocrine glands*

Chronologically, perhaps the first physiologic deficiency of aging which may affect operability is the decreased protein anabolism following the climacterium. In the aged, the main source of anabolic steroids is the adrenal gland.

Thyroid deficiency, as such, is not a fundamental part of the aging process, but there is a deficiency in utilization of oxygen at the cellular level. This deficient utilization is partially dependent on a decrease in available circulating thyroid hormone, because of a less efficient vascular system.

*Cellular metabolism—antibodies*

Generalized retardation of cell division is a fundamental physiologic difference between the young and the aged. Healing may be slower. Formation of antibodies against pathologic organisms may also be decreased.

*Decreased liver stores*

The aging liver has enough reserves to meet the stresses of a surgical operation. However, a dangerous decrease in the efficiency of the liver because of disease processes is relatively common in the elderly. In our local charity hospital, liver function tests are part of the routine work-up in the elderly surgical patient.

## SUMMARY

The importance of evaluating the organ systems is twofold: 1) to estimate the amounts of physiologic elements which can be replenished and restored in order to increase the safety of operation, and 2) to recognize the irreversible depletions, and to protect the body against further loss or exhaustion.

In general, if the aged patient is reasonably active physically, can walk upstairs without dyspnea, has no ankle edema or orthopnea and no renal dysfunction or urinary obstruction, then the least we can infer is that the three systems (cardiovascular, pulmonary and renal) which are so important to the economy of the body have enough reserves to meet the stress and strain of ordinary living. In turn, unless we prove otherwise, it is likely that the patient will be a reasonably safe risk as a surgical candidate.

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# VARIATIONS IN THE RESPONSE OF INDIVIDUALS OF DIFFERENT AGES TO AN ANTITHYROID COMPOUND (METHIMAZOLE)

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Variations with age in the gross appearance (1), histology (1–6), and function (1, 7–11) of the thyroid have been described. Indeed, McCay (12) states that "the decline in basal metabolism in old age has been recognized for nearly a hundred years." Gross changes in the size of the gland at puberty, with marriage and in the menopause have been recognized from ancient times (13). The normal thyroid apparently attains its maximum size, and possibly its maximum function, between the ages of 15 and 20 years (1). In the elderly, between the ages of 60 and 80, the gland is definitely reduced in size, the colloid is less rich in thyroxin (14, 15) and the blood supply is decreased (3, 16, 17). In conjunction with these involutionary changes, which begin about the age of 40 or shortly thereafter, nodule and cyst formations are common (18, 19). Considerable work has been reported which is concerned with the ability of hormonal materials to prevent or reverse these changes (20, 21). In view of these variations in thyroid structure and function in relation to age, observations have been made in 184 cases of hyperthyroidism in which methimazole has been employed to determine variations, if any, in the response of the hyperthyroid state, as influenced by age at the time of treatment.

## SUBJECTS AND METHODS

The procedures used in studying 184 patients with hyperthyroidism have been described in full elsewhere (22, 23) and will not be detailed here. Of the 184 patients, 35 were being prepared for surgery, and 147 were being given methimazole with a view to long-term treatment. Forty-three were hospitalized at the beginning of the therapeutic regimen, not because of the greater severity of the hyperthyroidism, but in order to carry out a more complete study of the effects of the antithyroid agent. On these patients, clinical observations were made and recorded daily; on out-patients, such records were made at weekly intervals. Subjective symptoms (such as apprehension, nervousness, irritability, inward trembling, and tension) and objective phenomena (such as tremor, excessive sweating, eye signs, hyper-reactivity, and changes in weight, blood pressure and pulse rate) were appraised at each visit. Determinations of the basal metabolic rate, serum total cholesterol level and blood count were performed once weekly in all hospitalized patients; they were made in all outpatient cases once weekly until control was established, and then at periods varying from two weeks to one month. In some instances thyroidal radioactive iodine uptake and/or serum

protein-bound iodine determinations were used to check the degree of control attained.

Of the 184 patients, 141 (76.6 per cent) were women; 40 (21.6 per cent) were men and in 3 the sex was not recorded. In age, they ranged from 15 to 83 years, with an average for the women of 41.6 and for the men, 40.3 years. In 98 of the 184 patients the thyroid was diffusely hyperplastic; in this group, 75 were women and 23 were men. A grossly nodular gland was palpated in 51 women and in 11 men. No thyroid tissue could be found in the neck of 4 men and 2 women, but was demonstrable substernally or intrathoracically. In 11 other patients, no thyroid tissue could be detected in the cervical region. The thyroid appeared to be normal on palpation in 3 women. The status of the gland was not recorded in 4 instances. Thyroidectomy had been previously performed in 20 subjects.

In order to ascertain the influence of age upon the action of methimazole, these 184 subjects were arbitrarily divided into three groups: Group I—those between 15 and 34 years, including 35 women and 11 men; Group II—those between 35 and 54 years, including 64 women and 20 men; Group III—those between 55 and 83 years, including 38 women and 7 men. In 9 patients the age was not recorded.

## RESULTS

The differences in the clinical behavior between the three age groups were studied in relation to (a) the time required to bring about an initial improvement in the hyperthyroidism, (b) the time required to gain complete control of the hyperthyroidism, (c) the changes observed in weight, pulse rate, pulse pressure, and serum cholesterol level, before and after control was established, (d) alterations in the size of the gland under therapy, and (e) the incidence of "cures."

### (a) *Time required for initial improvement in hyperthyroidism* (Fig. 1)

For this comparison, data were recorded in 150 instances, but in 32 the maximum daily dose of 20 milligrams of methimazole was not optimal. These patients were finally not included in the analysis. The remaining 118 patients received initial daily doses of from 30 to 40 milligrams. Although some patients stated that they had noticed relief of "inner tension" within twenty-four to seventy-two hours, improvement was not recorded until there was also a definite relief of some of the other presenting signs or symptoms, such as tremors, hyper-reactivity, excessive sweating, tachycardia, and alterations in appetite, bowel function, or sleep patterns. A decrease in the rate of weight loss was often among the first objective changes to be noted. Appreciable alterations in the basal metabolic rate and serum cholesterol level were rarely observed until other indices of improvement were already in evidence. There was no essential difference in the speed with which improvement occurred in cases of toxic diffusely hyperplastic goiter as compared with cases of toxic nodular goiter.

All of the 118 patients compared in Figure 1 showed unmistakable evidences of improvement within the first two weeks of treatment with methimazole. It may be seen that the youngest and oldest age groups responded more readily

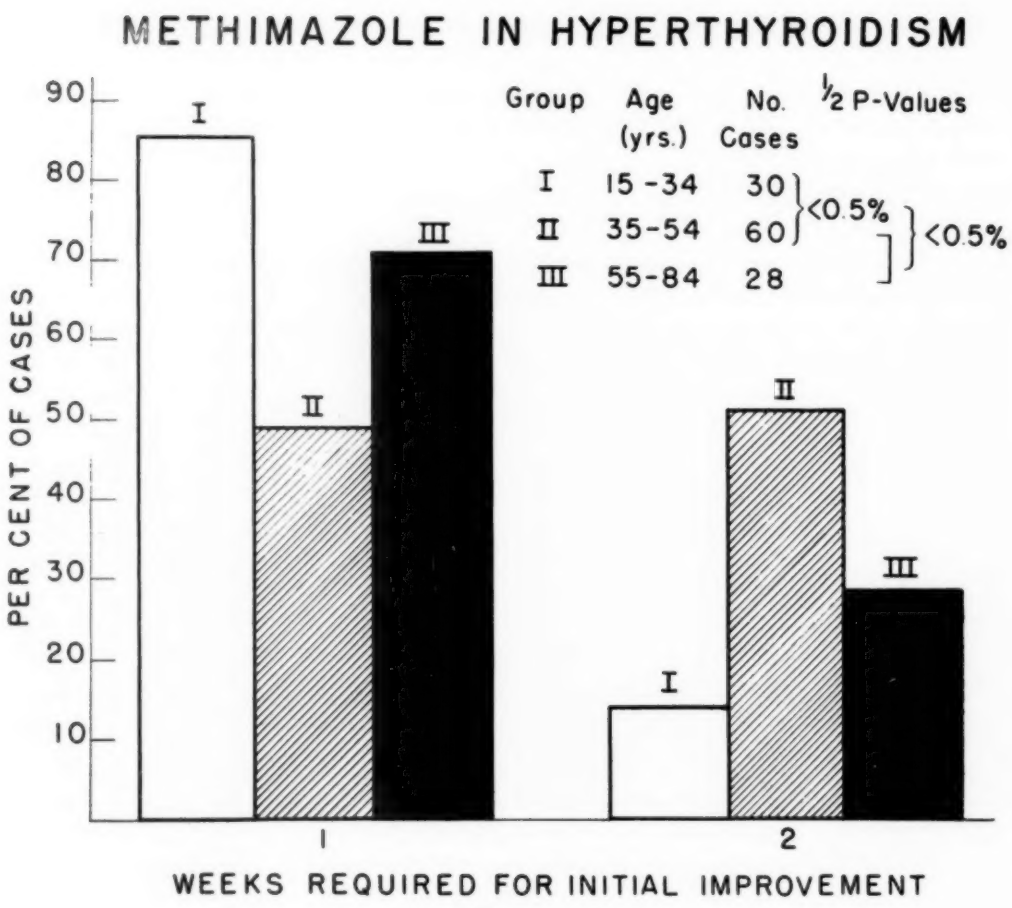


FIG. 1

than did the middle-age group. During the first week, in Group I there was evidence of improvement in 26 of the 30 patients (85.8 per cent); in Group II, in 29 of 60 subjects (48.3 per cent); and in Group III, in 20 of 28 individuals (71.2 per cent). These differences are statistically significant when Group I is compared with Group II alone, or in combination with Group III; the ½P value in both instances is less than 0.5 per cent.

(b) *Time required for control of the hyperthyroidism* (Fig. 2)

Observations on this point were made in 137 of the 184 patients, of whom 113 (82.4 per cent) were brought to a euthyroid state within five weeks after initiating therapy. Figure 2 is based upon data from 105 subjects who received daily a dose of 30 or 40 milligrams of methimazole until control was established. In 100 of these (95.2 per cent) the disease was controlled by the end of the fifth week of therapy. In Group I, control was established in 12 of the 28 subjects (42.8 per cent) by the end of the third week, in an additional 12 by the end of the fourth week, and in 5 by the end of the sixth week; in 1 instance the disease was never controlled (Fig. 2). In Group II, 17 of 54 patients (31.5 per cent) were euthyroid

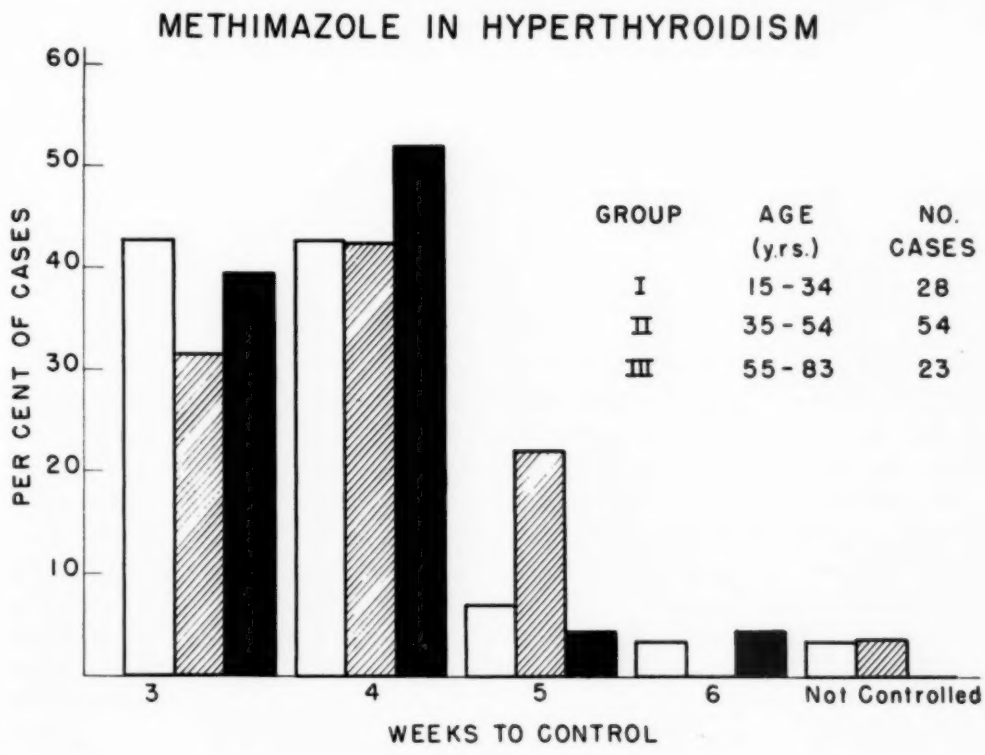


FIG. 2

by the end of the third week, an additional 23 became so during the fourth week, and 12 during the fifth week; in the remaining 2 the disease was never satisfactorily controlled with the dosages mentioned (Fig. 2). In Group III, 9 of 23 patients (39.1 per cent) were euthyroid by the end of the third week, 12 others (52.1 per cent) became so during the fourth week, and the remaining 2 by the end of the sixth week (Fig. 2). From inspection of Figure 2 one gains the impression that the subjects of Groups I and III came under complete control more readily than those of Group II. However, no statistically significant differences can be found between any of the groups or any combination of them. Nodular and hyperplastic goiters were controlled with equal readiness.

(c) *Variations in clinical findings* (Tables 1, 2 and 3)

At each visit of the patient, it was our custom to check not only changes in subjective phenomena and clinical signs but also to determine weight, pulse rate, blood pressure, basal metabolic rate, serum cholesterol level, blood count and, in selected instances, the serum protein-bound iodine level. Calculated in relation to age, the basal metabolic rates were within the normal range in all subjects in whom the hyperthyroidism was completely controlled. In the 125 subjects on whom determinations of serum cholesterol concentration were made, 99 showed a progressive increase in the value, 16 a decrease, and 10 no essential change. The direction and magnitude of the *change* were not significantly dif-

TABLE 1

*Changes in Weight of Thyrotoxic Patients of Various Ages Treated with Methimazole*

| Age group | Direction of change in weight | | |
|---|---|---|---|
| | Gain | Loss | No change |
| 15–34 | 38 | 3 | 2 |
| 35–54 | 63 | 9 | 8 |
| 55–84 | 33 | 5 | 3 |
| Age not recorded | 4 | 0 | 0 |
| *Totals* | *138* | *17* | *13* |

ferent when a group or combination of groups was compared with any other, nor did patients with nodular goiter behave in a materially different fashion from those with diffusely hyperplastic glands.

From Table 1, it would appear that there was a trend toward a higher incidence of *weight gain* in the subjects of Group I than in those of the other two age brackets. However, these differences had no statistical significance. It would have been interesting to study the gains in weight quantitatively, in relation to the optimal weight and to the amount actually gained in each individual patient of the three groups. It is our impression that patients with Graves' disease, and hence the younger subjects, tend to lose weight more rapidly and to a greater extent than the older thyrotoxic subjects.

In Table 2 are segregated by groups the numbers of individuals who had *pulse rates* above 88 per minute before treatment, and below 88 after the thyrotoxic state was controlled. In 146 of the 184 patients to whom methimazole was given, such pretreatment levels were obtained. Of the remaining 38 subjects, 21 in whom the disease had previously been controlled by another antithyroid compound prior to the use of methimazole were not included in this analysis; among the other 17, age was not recorded in 9, and in 7 the pulse rates were below 88 per minute despite the presence of recognizable thyrotoxicosis. In the three groups respectively, beginning with the youngest (Group I), there was a reduction to within the normal pulse range in 35 of 40, 53 of 72, and 19 of 34 subjects. The behavior of the first group is significantly different from that of either of the two remaining groups or from these two in combination ($\frac{1}{2}P$ between 0.5 and 2.5 per cent).

TABLE 2

*Variations in Pulse Rates of Thyrotoxic Patients Treated with Methimazole*

| Age group | Pulse above 88 beats/minute | | ½P. values |
|---|---|---|---|
| | Before treatment | After treatment | |
| 15–34 | 40 | 5 | Between ½ and 2½% |
| 35–54 | 72 | 19 | |
| 55–83 | 34 | 15 | |
| *Totals* | *146* | *39* | |

TABLE 3

*Changes in Pulse Pressure During Therapy with Methimazole**

| Age group | Total No. of patients | Before treatment | | After treatment | |
|---|---|---|---|---|---|
| | | Above 60 mm. Hg | Below 60 mm. Hg | Above 60 mm. Hg | Below 60 mm. Hg |
| 15–34 | 42 | 29 | 13 | 3 | 39 |
| 35–54 | 73 | 50 | 23 | 14 | 59 |
| 55–80 | 38 | 31 | 7 | 20 | 18 |

* Excludes all patients known to have had high blood pressure prior to onset of disease.

The trend of the pulse toward normal levels was noted more often in the young than in the two older groups. This difference was statistically significant when the youngest group was compared with the oldest but not for any other comparison, separately or in combination.

In Table 3 are listed 153 patients who were believed not to have had high *blood pressure* or a high *pulse pressure* prior to the onset of hyperthyroidism. In all of these cases, the reduction of pulse pressure under treatment was the net result of a decrease in systolic, and an increase in diastolic pressure. In Group I, of 29 patients with a pulse pressure greater than 60 mm. of mercury before treatment, a reduction to normal levels accompanied methimazole administration in 26. Similarly, during treatment, 36 of 50 subjects and 11 of 31 subjects in Groups II and III, respectively, showed a lowering to normal of previously high values. These changes are statistically significant for comparisons between Groups I and III ($\frac{1}{2}$P is less than 0.5 per cent), between Group I and a combination of Groups II and III ($\frac{1}{2}$P is between 0.5 and 2.5 per cent), and between Groups I and II combined as compared with Group III ($\frac{1}{2}$P is less than 0.5 per cent).

(**d**) *Alterations in the size of the thyroid* (Fig. 3)

In 90 of the 184 patients studied, a record was kept of alterations in the size of the thyroid while under treatment with methimazole. Unfortunately the age of 6 patients was not recorded. In Figure 3 are shown the essential data for the remaining 84. It is true that the data in this figure are weighted, since a failure to mention alterations in glandular size or configuration may mean either that they did not occur or that they were not of sufficient magnitude to attract the attention of the physician, patient or patient's family. The initially enlarged gland decreased in size in 15 of the 23 cases in Group I; in 16 of 37 cases in Group II, and in 10 of 24 in Group III (Fig. 3). The larger number of subjects with a diminution in the size of the gland in Group I as compared with either of the other groups was probably related, at least in part, to the higher incidence of diffusely hyperplastic glands in this group (78.3 per cent, as compared with 59.5 and 41.7 per cent in Groups II and III, respectively). The differences in size from group to group do not have any statistical significance within the 5 per cent level of confidence. However, with age, there seems to be a decrease in the capacity of the gland for growing smaller as toxicity disappears. This decrease is probably due to the gradually lessening blood supply, an increasing amount of connective tissue and the greater incidence of nodules.

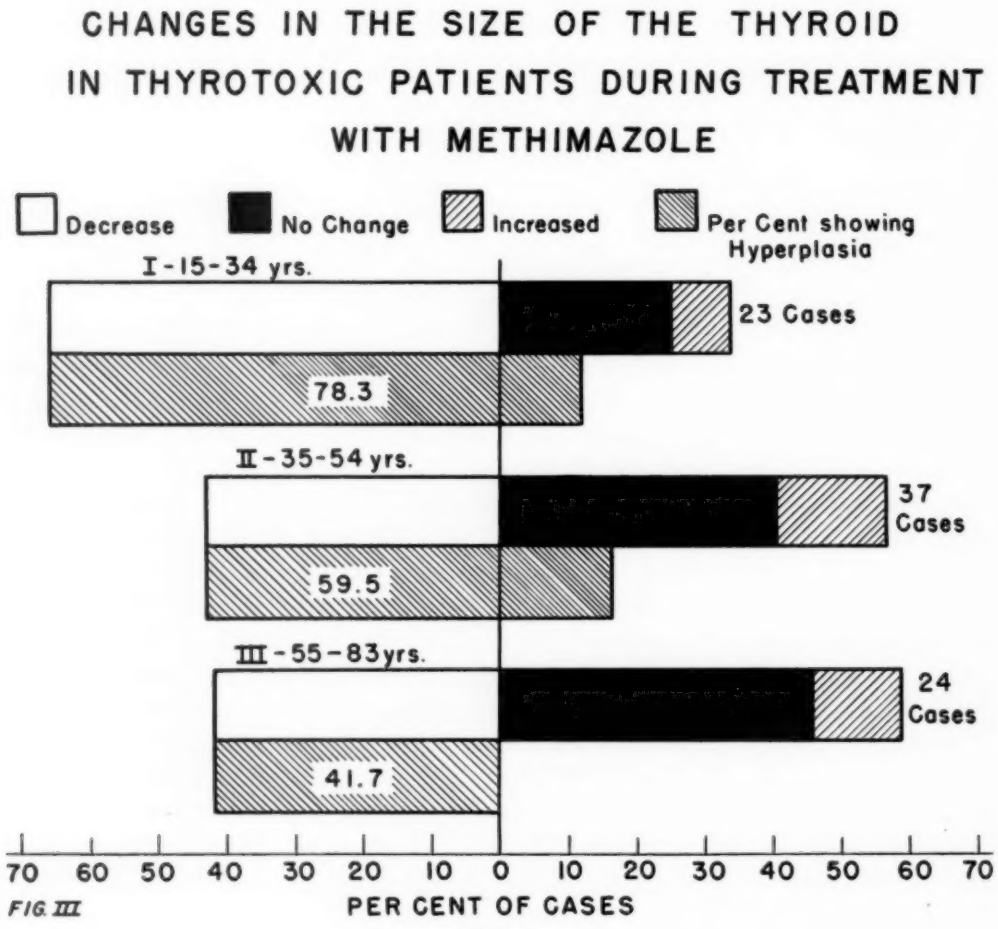


FIG. 3

(e) *Incidence of "cures"* (Table 4)

The final disposition of 133 of the 184 cases of hyperthyroidism treated with methimazole is as follows: 37 were prepared immediately for operation; of the remaining 96, 41 were still receiving methimazole therapy when the present study was closed. This left 55 patients in whom the long-range effects of methimazole could be analyzed. In 34 of these (61.8 per cent) the results have been

TABLE 4

*"Cures" in Thyrotoxic Patients Completing a Course of Therapy with Methimazole*

| Age group | Total No. of patients | "Cures" | |
|---|---|---|---|
| | | Number | Per cent |
| 15–34 | 17 | 13 | 76.5 |
| 35–54 | 23 | 14 | 60.9 |
| 55–83 | 15 | 7 | 46.6 |
| *Totals* | *55* | *34* | *61.8* |

considered as "cures" or recoveries. This is undoubtedly a weighted figure, as it must be presumed that at least some of the 51 cases not followed received other therapy. If we assume that all of them did, then the percentage of cures drop to 32.1 per cent. The actual figure probably lies somewhere between the 32.1 and 61.8 per cent. From Table 4, it will be seen that there is a tendency for the percentage of cures to decrease with age. There were no differences significant within the 5 per cent level of confidence.

## DISCUSSION

The differences that have been observed in the action of methimazole in patients of various ages may be related 1) to the variations in the natural course of hyperthyroidism, 2) to the nature of the pathologic condition in the thyroid, 3) to the changing endocrine pattern, or 4) to alterations in the reactivity of the individual with increasing years.

Perhaps the higher percentage of "cures" in the youngest age group is related to the higher incidence of Graves' disease and its nearly constant association with emotional or mental stresses—factors which seem to exert less influence upon the nodular goiters of older individuals.

Some of the factors influencing thyroid-gonad relationships have been summarized earlier (24). More recently (25) attention has been called to the high incidence of ovarian disease in patients who have had, or will develop an alteration in the thyroid gland. That the middle-age group responded more slowly than either the older or the younger groups may support the concept that the menopause is a period of glandular adjustment in which it is more difficult to achieve or to maintain normal thyroid function.

In the present series, the type of gland (*i.e.*, whether diffusely hyperplastic or nodular) seems to have played little part in the final results, nor to have materially influenced the speed with which the thyrotoxic state could be controlled by the antithyroid compound. However, the diffusely enlarged glands of Graves' disease were observed to decrease in size more frequently than the nodular goiters. Astwood and his associates (26) believe that prolonged remissions are associated with a decrease in the normal size of the thyroid while the patient is under treatment, followed by a return to normal after the antithyroid compound is discontinued.

Irwin, Van Vactor and Norris (27) feel that the length of time required to bring the patient to a euthyroid state varies directly with the size of the goiter. Bartels (28, 29) and Kendrick, Balls and Rose (30) are of the opinion that with antithyroid compounds it takes longer to control the nodular than the diffusely hyperplastic goiter. On the other hand, the present data, and our own experience with antithyroid compounds (31, 32, 33) are in accord with the conclusion of Hallman and Bondy (34), who state that neither a longer period of time nor a larger dose of drug are necessary to control toxic nodular goiter as compared with toxic diffuse hyperplastic goiter.

## SUMMARY

For 184 thyrotoxic patients undergoing treatment with methimazole, data have been analyzed in relation to three age groups, namely, I (15 to 34 years),

II (35 to 54 years), and III (55 to 84 years). Initial improvement was first noted in Group I, and control of the thyrotoxic state was more readily established in Groups I and III than in II. During treatment with methimazole, patients in Group I gained weight more readily than those in the other two groups, but they also lost more easily when out of control. A return to normal in pulse rates, and systolic and pulse pressures was more rapid in Group I than in Groups II and III. A reduction in the size of the initially large gland was most frequently encountered in Group I. The percentage of "cures" or recoveries following an adequate course of therapy was highest in Group I and lowest in Group III, but the observed differences were not statistically significant within the 5 per cent level of confidence.

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# NEW TRENDS IN THE TREATMENT OF FRACTURE OF THE HIP IN THE AGED*

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Many authors have designated fractures of the hip as the unsolved injury. Since remarkable progress has been made in the treatment of various complications of this injury in recent years, such a generalization is misleading. Today there is a high percentage of good results (1–12). The important step in improvement in the management of this fracture seems to be the individualization of treatment, and the proper selection of cases, taking particularly into consideration pre-existing local or constitutional pathologic conditions, the age of the patient and the type of fracture line. The three main surgical methods available for the treatment of this injury are:

A. Internal fixation with a Smith-Petersen or other type of nail.

B. Excision of the femoral head and the introduction of a prosthesis.

C. Primary osteotomy.

Primary osteotomy, suggested for fractures from a shearing stress, is not suitable for the very aged because it has the great disadvantage of requiring three to four months of non-weight-bearing and protection before healing occurs.

The purpose of this paper is to study two series of personally treated patients. One group represents 100 cases treated by internal fixation with Smith-Petersen or other nails; and the other, 22 cases of fracture treated by the use of a metal prosthesis following excision of the femoral head.

## MORTALITY

By studying these two groups it was felt that the proper application of each method could be found. In comparing the complications and disadvantages of each procedure we found that the mortality for the pinning operation was 9 per cent, which is comparable with mortalities given in other recent reports (Table 1). It is significant that in 38 patients under the age of 70 operated upon, there were no deaths; and that 6 of the 9 deaths recorded after the age of 70 followed complications not demonstrated for from three to five weeks after operation (Figs. 1 and 2). These complications seem to have been due in part to the restriction of the patient's activity, in spite of meticulous effort to give bed exercises. Persons between 80 and 90 years of age represent a group that might be better treated by introduction of a prosthesis which allows immediate activity. In passing, it should be mentioned that one of the great steps forward in treatment of fractures of the hip has been the appreciable reduction in mor-

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TABLE 1

*Mortality Rates*

| Authors | No. of cases | No. of deaths | Percentage |
|---|---|---|---|
| G. E. & R. E. Van Demark | 104 | 14 | 12.2 |
| Stewart & Alfano | 41 | 8 | 19.0 |
| Moore | | | 10.0 |
| Boyd & George | 300 | 28 | 9.3 |
| Manchester Royal Infirmary (Willis) | 192 | 15 | 8.0 |
| Report of A.A.O.S. (1941) | 923 | 107 | 11.0 |
| Soto-Hall & Lillo | 100 | 9 | 9.0 |
| Total | 1660 | 181 | 10.9 |

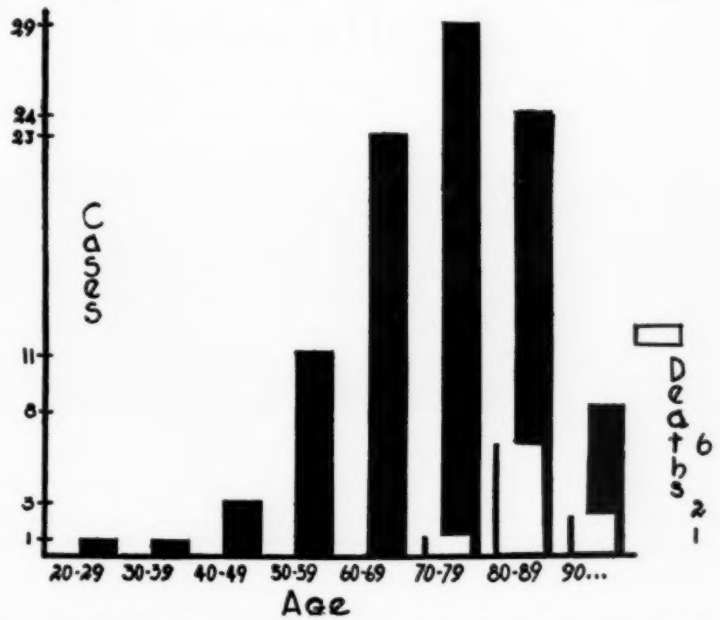


FIG. 1. Mortality statistics: 100 cases of internal fixation of the hip with Smith-Petersen or similar type nail. The deaths occurred in patients over 70 years of age.

tality compared to that following simple reduction and immobilization in plaster, which carried a death rate approximating 35 per cent.

## INTERNAL FIXATION

One of the complications of the nailing operation is displacement of the nail. This was noted in 5 of our elderly patients, and was found mainly in subcapital fractures in which the head fragment was too small to allow adequate fixation. Figure 3 shows the height of three femoral heads which had been excised at operation. It is obvious that the fragment is too small to be gripped properly and immobilized by the pin. Often the bone itself is too fragile and the pin works out through one side, as noted in two of these heads.

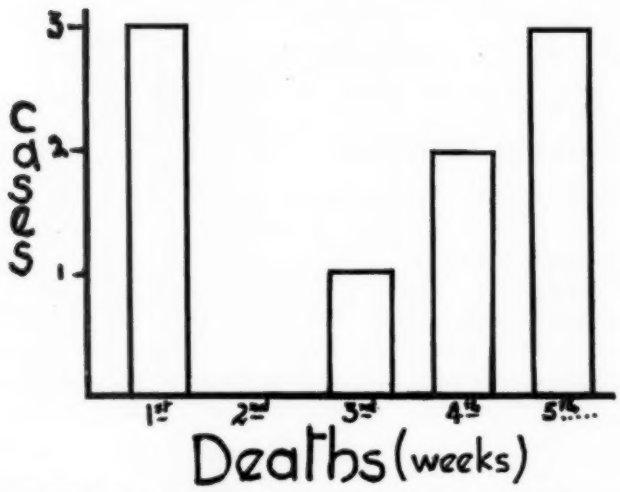


FIG. 2. Postoperative time of death in 9 cases, following nailing operations. Note: 6 of the 9 patients died with complications which appeared three to five weeks after operation.

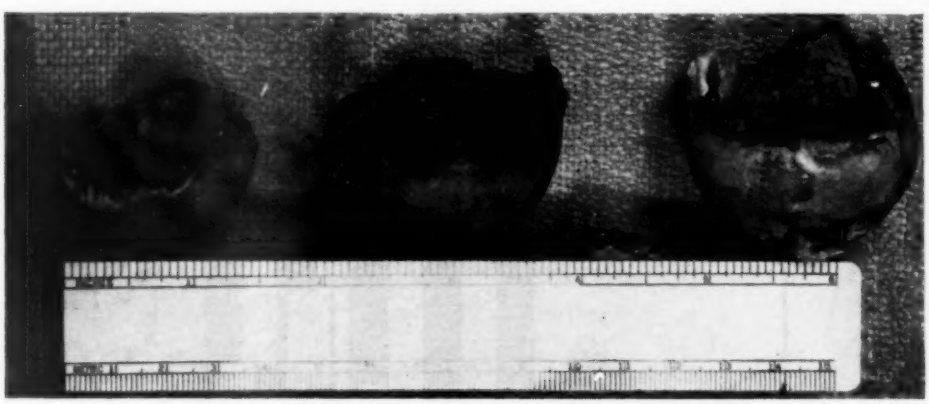

FIG. 3. Femoral heads excised after displacement of Smith-Petersen nail. Eroded areas show where nail had broken through. These proximal fragments are too small for proper gripping of the head.

Two other major complications of the pinning procedure are 1) the failure of union of the fracture and 2) the development of avascular necrosis of the head, with or without union. Adequate bony union cannot be demonstrated clinically or radiologically for at least four or five months in true neck fractures. Avascular necrosis may not develop for from six months to two years after the injury. Thus many months must elapse before the patient can become ambulatory. Such a period of time may represent a considerable part of such a person's life expectancy. The incidence of avascular necrosis of the femoral head is rather high, particularly in the older individuals. The general average, from reports by various authors, is 26.5 per cent (Table 2). Of course avascular necrosis occurs much more frequently in subcapital fractures, in which there also is a high percentage of nonunion. In general, 1 hip fracture in every 5 fails to unite, as shown by the statistical studies in Table 3.

TABLE 2

*Avascular Necrosis*

| Authors | Total cases | No. of cases of avascular necrosis | Percentage |
|---|---|---|---|
| McCarroll | 203 | 60 | 29.5 |
| Boyd & George | 122 | 40 | 33.6 |
| Christophe, Howard, Potter & Driscoll | 83 | 16 | 19.2 |
| Report of A.A.O.S. (1941) | 105 | 20 | 19.0 |
| Total | 513 | 136 | 26.5 |

TABLE 3

*Nonunion*

| Authors | Total cases | No. of cases of nonunion | Percentage |
|---|---|---|---|
| McCarroll | 203 | 50 | 24.6 |
| Boyd & George | 300 | 40 | 13.5 |
| Christophe, Howard, Potter & Driscoll | 83 | 13 | 15.6 |
| Report of A.A.O.S. (1941) | 144 | 39 | 27.1 |
| Total | 730 | 142 | 19.4 |

## PROSTHESIS

Local complications, such as avascular necrosis and nonunion, which necessitate many months of restricted activity before they can be treated surgically in individuals with a short life expectancy, point to the need of developing a new therapeutic approach. In 1946 Judet published the first case of excision of the femoral head with prosthetic replacement. The result was considered good and in his book he reported that some three years later the condition of this patient was found to be excellent. Since then many authors have reviewed small series which, unfortunately, have not been followed for a long enough period.

Indications for the use of a prosthetic substitute seem to be divided into local and general factors. Local indications are 1) high fractures (subcapital), in which the fragment is too small to permit an adequate grip with a pin, 2) fractures with a shearing stress—a group which often shows a high percentage of nonunion, and 3) pre-existing local disease, *e.g.*, osteoarthritic deformity or severe osteoporosis.

Of the constitutional indications, among the more important are 1) senility, with difficulty in controlling activity of the patient, 2) pre-existing disease such as Parkinsonism, which often dooms pinning to failure, 3) psychoses, and 4) patients over the age of 75. In our series of 22 fractures treated by the introduction of a metal prosthesis, the patients' average age was 73. This low average age was caused in part by 2 patients under the age of 60; prosthesis was used in these 2 instances because the patients were psychotic and had sustained hip fractures during shock treatment.

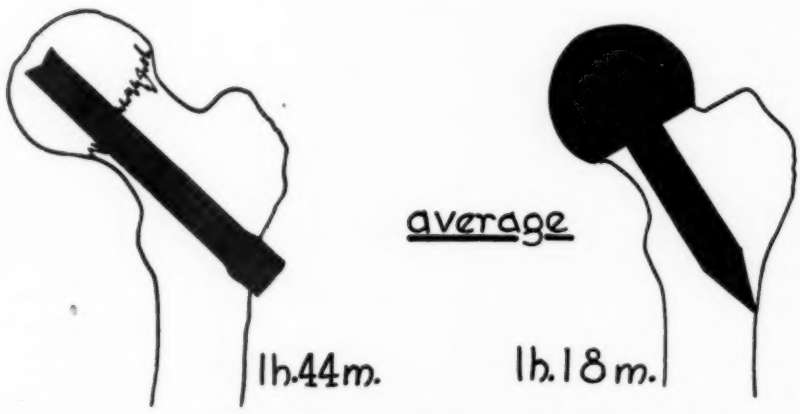


FIG. 4. Operative times for nail-fixation (left) *vs.* prosthesis (right). Longer operative time in nailing operation is due partially to need for roentgenologic studies during procedure.

In reviewing the complications in this operation it should be noted that the operative time is often shorter in the Judet procedure (an experience which also has been reported by other authors (Fig. 4)) because it eliminates the delay necessary for making x-ray studies in the pinning operation. The anesthetic is well tolerated in the Judet procedure. Anesthetists state that there seems to be less stress in the replacement by prosthesis than in the operation by internal fixation with pins. Perhaps this may be accounted for by the prolonged period necessary to maintain an aged patient in a fixed position on the fracture table while introducing the pin.

In our series no local complication such as sepsis was encountered and there were no deaths. There was displacement of one prosthesis, apparently produced by the breaking of the soft, fragile bone of the femoral neck. Vaughn-Jackson has treated 34 patients (average age, 75) treated by the same method with only 1 death. This experience would suggest that the operation is well tolerated by patients in this age group.

With a prosthesis in place, patients show remarkable freedom from pain. Within a day, passive movement of the leg is possible and within a few days patients are able to elevate the leg actively, and can sit up and breathe without difficulty. Of great importance is the time element in weight bearing. With a prosthesis, weight bearing can be started very early, and thus the deleterious effect of recumbency can be combated. Our patients become ambulatory with help within two or three days. Within six to eight weeks they should be able to get around the house and perform many of their household duties if their general condition allows it. The period of hospitalization is appreciably reduced, due to this freedom of activity.

One of the arguments against the use of a metal prosthesis has been that we do not know whether the prosthetic device will continue to be well tolerated in the future. There appears to be some wear and tear and absorption of the femoral neck with the passage of time. The metal itself is inert and produces no

FIG. 5. Prostheses used in authors' series of cases.
Left: cup-shaped prosthesis with three-flanged nail at center (Naden-Reath type)
Right: authors' modification. Additional lip which projects into greater trochanter, to give additional stability and increase weight-bearing surface.

tissue reaction. Our experience in the use of Smith-Petersen metallic cups for mold arthroplasty gives some indication of how long a cup may be present without adjacent bone change. Several of our patients have had cups in place for thirteen and fourteen years; apparently these cups withstand stress and strain without deterioration in the hip.

We have now observed prosthetic femoral heads for as long as two and a half years and, although there has been some slight increase in pain reported by certain patients, no appreciable break-down of the hip has been noted. Very few patients have had perfect results and some 90 per cent have a slight degree of pain. In fracture of the hip, however, we are confronted by a serious crippling lesion, which often leads to fatal complications. Thus if we can obtain a stable, movable hip and early ambulation, despite slight pain, introduction of a prosthesis would seem to be the procedure of choice.

## SUMMARY

In cooperative patients under 75 years of age with transcervical or cervicotrochanteric fractures of the hip a Smith-Petersen pin or other type of adequate nailing should give a high percentage of successful results, with practically no mortality. Patients over 75 years of age with high fractures should not be allowed to wait a matter of months or years in order to determine the success or failure of a pinning operation, and be subjected to the frequent complications associated with this type of treatment, for often these fractures are only a part

of the general pathologic condition leading to the injury. It is likely that better results will be obtained by the immediate application of a femoral head prosthesis.

Guiding principles in the surgical treatment of hip fracture involve: 1) adequate internal fixation, when possible, in middle-aged patients, and 2) immediate use of a replacement prosthesis, in older patients in whom general complications or local factors clearly demand early ambulation.

Success in the future treatment of fractures of the femoral neck will come from continued individualization of surgical therapy.

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# MANAGEMENT OF HIP FRACTURE IN THE GERIATRIC PATIENT*

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The brass cuspidor, the roll-top desk, the scrolled and lettered black iron safe, the padded and studded swivel chair, the high oaken bookkeeper's perch—these were the typical office of a recent era. At the same time treatment of the older individual with a hip fracture was characterized by sandbags, long periods of recumbency, bedsores, low morale, a high mortality rate and often an extremity unfit for satisfactory function. The management of the office and the management of hip trauma have undergone mutation dictated by the desire to improve the final result in each instance.

Trauma to individuals in the higher age groups has increased and the reason lies chiefly in the rise in the geriatric population. Better living and health measures have brought about the increased number of older patients. This is the same age group that presents the clinician with decreased height, atrophy of various structures, circulatory disturbances and a host of other conditions possible only in the victim of physiologic senescence. In reviewing our series of hip injuries, we found that approximately 80 per cent occurred in patients beyond the age of 60 years. In most instances such a fracture reflects a general physiologic debit which is manifested in the skeletal structures by degrees of demineralization. This mineral deficiency provides vulnerability to injury resulting in fractures.

The goal in managing trauma to the hip is the restoration of the patient to full functional capacity by the earliest, most comfortable means. Three broad categories should be considered, and the problems in each must be overcome successfully in order to reach the defined goal. These categories may be listed as mental, physical and vocational in scope. The word "rehabilitation" is avoided, since it is felt that all phases of treatment are an integral part of the rehabilitation of any patient.

## MENTAL FACTORS

An early mental problem is met in many patients who have a false impression that nothing can be done for them. A depression state is not uncommon and is often the result of gossip or the memory of the loss of a relative or friend under similar circumstances. Most patients do not hear of the good results by this same gossip method, or else they forget them. Reassurance is an early part of the management and is made easier by explaining the pathology of the condition, using terms the non-medical individual can understand. The plan of treatment

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should be outlined and the patient's role stressed in the convalescent period. He should be made to feel that he is part of a team—as he surely is. Failure to minimize insecurity and enlist patient cooperation can result in a defeatism which will make management most difficult and at times impossible. Defeatism can be a part of the physician's attitude too. It should be studiously avoided, since the patient's state of mind has little chance of getting beyond a depression state under such circumstances.

Disorientation, memory defects, emotional lability, and periods of confusion are not uncommon in the few days following injury. These may result from the shock of the sudden change in life, and not necessarily from surgical shock. A second cause is the presence of fat emboli arising from the fracture site, and such a possibility must always be kept in mind. Fat emboli may be reduced by early operation on the hip, since the surgical wound provides an exit for the free fat and reduces the possibility of further emboli. Other medical states may cause disorientation and some of these may precede the injury. A careful history will bring out these facts.

Constant encouragement is necessary in the geriatric patient—to a greater extent than in younger age groups. Often the daily visit by the physician is a sufficient morale booster. Hope of recovery should be instilled at all times, even though there are facts to the contrary. Attention to comfort, diet, bowel function and sleep habits helps to provide security for the patient.

## PHYSICAL FACTORS

Physical factors make up a large part of the management of hip fracture. These include circulation of the hip, quality of bone and soft tissue, medical inventory of systems, and reduction and fixation of fragments.

The circulation of the hip joint is generally poor, hence there is little reserve to withstand the effects of disease or trauma. When the blood supply is less than normal for a considerable time, the bone structure is apt to become so weak that a fracture will occur under stress, even though there has been no fall. In a recent case, the patient merely reached down to tune his television set and the femoral neck gave way. No pathologic lesion could be demonstrated. On the other hand, an injury may cause loss of continuity of the femoral neck and the vessels supplying the femoral head. Blood supply is often altered to such a degree that survival of the femoral head is unattainable, regardless of the type of treatment rendered. It is impossible to determine viability of fragments at an early date by any examination or x-ray means. One patient in our series showed histologic changes of early necrosis on the fifth day after injury, signifying that loss of circulation can start an immediate reaction of degeneration. Herein lies a major problem. It is most important to realize the possibility of necrosis of the femoral head, to watch for it and, above all, to do something about it when it is recognized. There is no excuse generally for noting the appearance and progress of such changes, and then acting as an observer of monthly x-ray films instead of changing the course of treatment. Undue loss of time in this manner will delay and impair the final result.

Osteoporosis is common, and the cause not specifically known. We read of the

man isolated on a raft for two months who eats the fish he is able to catch and drinks water with a high salt content. We read further that he is rescued, collapses and is found to have profound demineralization of the spine and collapse of several vertebrae. He has had a dietary demineralization. Many adults not confined to a raft deprive themselves of minerals because of a dislike for, or an intolerance to milk. Others who drink milk are not able to take advantage of the minerals, because of an achlorhydria or reduced acid content of the stomach. Osteoporosis is the result of a deficiency of, or a failure to assimilate minerals. It is not uncommon to find widows who exist on an irregular carbohydrate diet, largely because the family that was once present to demand meals is no longer on the scene to stimulate regularity and variety in the menu. In these individuals protein deficiencies develop which are often impossible to reverse. Diets containing adequate protein are helpful. The method of administering milk may be altered by adding 10 centimeters of dilute hydrochloric acid to a quart of milk. The patient is asked to drink two to four glasses of this mixture daily. Acid administered in this manner appears to be more efficacious than when given by other methods. The teeth must be protected from staining, by the use of a straw and a follow-up mouth rinse. Obese patients may use skimmed milk. Prepared mineral medication is given each patient in addition to the milk in the diet.

Cardiac, genito-urinary and gastro-intestinal diseases are apt to be present. Prolonged recumbency may bring forth latent symptoms which may greatly alter the course of treatment. If the possiblity of complications arising from these factors is kept in mind, they can be checked early.

Nursing care to prevent the formation of decubiti is essential. This should include some movement of the patient, strict attention to care of the skin on the back and buttocks, and the elimination of wrinkles in the mattress and the covering of the rubber pad that usually is situated just under the sheet. Talcum powder to the back and bed absorbs much perspiration and reduces friction between the patient and the bed sheet. Friction alone may damage soft tissues enough to produce a large ulcer.

A physiologic reason for the breakdown of soft tissues is found in the inability of these tissues to withstand pressure, because of poor elasticity and poor circulation. Protein-deficient diets may lower tissue resistance to pressure or contusion.

Adequate reduction of fractures in general is felt to be necessary in order to gain healing, and the hip is no exception. Actually reduction should be particularly accurate in this area. The so-called impaction fracture is really an impalement of fragments and, if too much emphasis is placed on the "impaction," disappointment can follow when absorption occurs around the fracture a few days later and allows the fragments to separate. These injuries should be treated surgically, as soon as the patient's general physiologic state has been determined to be satisfactory. When the patient's general condition is unstable, it is wise to wait until such time as no undue hazard exists. In some instances the fracture itself may be a complicated type that should not be treated by open operation, but submitted to immobilization in traction or a plaster-of-paris spica cast.

One of the most important features of the surgical approach is the anesthetic

phase. Poor anesthesia may breed disaster. Pre-medication should be used sparingly; usually atropine alone is sufficient. Narcotics in heavy doses are to be avoided. Hypoxia must be prevented, regardless of the type of anesthetic agent used, and regional supplementation is often very helpful in reducing abnormal reflexes in the patient. Regional anesthesia alone is the choice of some surgeons.

## VOCATIONAL FACTORS

Vocational aspects of the management of hip fractures begin immediately. An attempt should be made to keep the patient as active as possible under existing conditions. After reduction and immobilization of the fragments, physical activity should be encouraged as early as the day of operation. Exercises in bed are important. Deep breathing should be undertaken at intervals to prevent atelectasis. Exercise of the normal extremity can be carried out in bed, resulting in improvement of functional capacity of the muscles of that extremity, and at the same time a similar although less significant change in the injured extremity. This has been demonstrated by Dr. F. A. Hellebrandt, who supervises the activity program outlined for our patients. In order to be effective, these exercises should be carried out at frequent intervals during each day. Cardiac deficiencies may alter the indication for physical therapy of this type in bed.

Sitting on the bedside, and early use of parallel bars, walkers or crutches are activities which should be started as soon as the individual case permits. Graded limited weight-bearing exercises may be instituted as early as three weeks after operation in selected cases. Pressure on the floor by the foot of the involved side, amounting to 25–30 pounds is permissible immediately, without actual body weight bearing, since these figures approximate the weight of an average lower extremity. By touching the forefoot to the floor while the foot is bearing this amount of weight, it is easier for the patient to balance when using walking aids, and no damaging stress is passed on to the hip joint.

Early ambulation improves the patient's morale, eases nursing care, improves circulation of the structures about the hip, promotes healing and maintains function of the other joints. Many complications are likewise avoided.

## SUMMARY

The management of hip fracture in the geriatric patient should aim at getting the best functional result in the shortest time possible. The surgical approach has been a definite advance in this direction. Undesirable features such as immobilization with sandbags, long periods of recumbency, decubiti, deformity and other complications have been materially reduced by improvements in treatment. In spite of these changes, problems continue which we hope will be solved in the years to come.

# THE IMPORTANCE OF GERIATRICS IN INDUSTRIAL MEDICINE*

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The social, economic and philosophic aspects of aging have been discussed since the stone age. In 48 B.C., Cicero in his De Senectute emphasized the effect and inequalities of withdrawing old men from employment. Despite the long-time recognition of the problem concerned with aging, only recently has medicine applied the principles now known as geriatrics. The phase of medicine in which this application is most necessary—in fact, obligatory—is industrial medicine. Yet the implementation of a sound geriatric program in industry is going to be most difficult. In presenting the reasons for this I must necessarily be highly critical of those who intentionally or unintentionally create road blocks.

## THE PHYSICIAN

In the first place, most physicians feel they are not identified with, or do not want to be identified with industrial health. Holding to a narrow concept, they do not appreciate that the basic principle of industrial medicine is prevention. Busily engaged within their own medical domains, they are not aware of industrial medicine's program of early detection of tuberculosis, cancer, diabetes, epilepsy, emotional states, and heart and vascular disease. They do not know that real functional rehabilitation originated in industry, as did the improvement of the nutrition of the great mass of the American people; or that obesity has been attacked more effectively in industry by means of health counselling. All this is a far cry from finger wrapping or insurance medicine. If the physician at large is ignorant of our program, how is he going to participate in a geriatric regimen for the older worker, even though those concerned are also his patients. Yet without his participation no geriatric program in industry can be successful, since we do not have enough industrial physicians.

## THE EMPLOYER

The second road block is management. During World War II we heard the older worker praised for his low incidence of absenteeism, and his sense of loyalty, responsibility and experience. All this was said when the labor barrel was nearly empty. With the return of our fighting men and the opportunity to obtain a more vigorous worker, the older one was discarded to the human scrap heap. To any indictment I make of management there are, of course, exceptions. Certain of our large industries, with wise medical direction and good industrial relations, make every effort to retain their older workers. It must also be kept in mind that small plants employ the greater portion of our laboring force.

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We find too often an employer unwilling to shift a young worker from a light job so that an older man can continue his employment. He feels it is too much trouble and disturbs all phases of routine, even down to the bookkeeping of the payroll deductions.

Discharging the older worker after he has been absent due to illness is too common. His place has been filled by a younger man; perchance the job may still be open, but the illness has rendered the older man less capable. He requests a lighter job, but some young executive with no compassion in his heart resorts to the old dictum—"we just don't have any light jobs."

Retaining the aging but still capable employee entails overcoming the traditional retirement-age question.

As to hiring a new worker of 45 years of age or more, management often resorts to the aforementioned objections. In addition, management fears its liability for injury to older workers. It believes it is unprofitable to employ them because of the investment in training for a new job. Pension plans constitute a frequent reason for the refusal to hire the aging applicant.

## LABOR

Let us now turn to the attitude of labor. As one who for nearly twenty years has limited his practice entirely to occupational medicine, I have a deep appreciation of the benefits of intelligent unionism, and do not question the reason for its existence. On the other hand my relations with the individual workers have also revealed that unions often create hardships for the members they supposedly defend. The union's position regarding seniority, down-grading, reassignment of work and other rigid principles may seem just to its membership in the aggregate, but the failure to relax for individual cases cannot be supported. The unions' unwillingness to compromise in certain situations creates a hardship, especially for an older worker. In my work I see evidence of this daily. The following quotation from a previous paper (1) illustrates the point. "A mechanic with moderately elevated blood pressure went from one plant to another seeking employment. He was turned down because of this moderately elevated blood pressure. He is a victim of circumstances not of his own doing, nor can he justifiably blame management. Labor has insisted upon the broadest interpretation of the Workmen's Compensation Law. Undoubtedly in a spirit of trying to secure the greatest benefits for the working man, labor has unwittingly placed itself in a position similar to the Australian who tried to throw away his boomerang."

"Over the years labor has insisted upon increasingly broader interpretation of the Workmen's Compensation Act. Granting justification for this attitude in some instances, it must also be admitted that certain changes which seemingly benefit the mass, also result in an injustice to an individual worker. A demand or bargaining victor for a principle which applies to fifty thousand members may seem beneficial to a large group, but if it works a hardship on an individual then there should be some means of acknowledging the exception."

Leggo (2) in quoting this opinion of mine, states: "The opinions expressed in these quotations are compatible with my own opinion but the trend in industry

may be increasingly to reject for employment applicants who present physical difficulties, particularly the potentially more serious defects of increasing age, in spite of the fact that executives, as individuals, may be at the same time becoming more and more conditioned toward the belief that aging people can be and should be usefully employed. This apparent discrepancy in the attitudes of executives may be explained by their fear of paying the penalty of a continuing monthly compensation award and/or the assessment of a large-lump-sum award because of a trivial or minor injury. Thus, while believing personally that the older person can be useful and should be employed, administrators fear the threat of potentially great costs for a short-term employment."

## SUMMARY

It is apparent that interest in the employment problems presented by the aging and aged is increasing. One particularly notes programs devoted to occupying the time of the *retired* person. Community, church, fraternal and even trailer-court groups are surprisingly active in entertaining the retired.

Likewise a perusal of the program for this year's meeting of the American Geriatrics Society reveals that the internist, surgeon, endocrinologist, gynecologist and others consider the age factor as they render treatment. It must be said, however, that few or none of these specialists or the general practitioner are appreciably or sufficiently concerned with the working environment of their elderly patients. The traditional advice—"you should stop working," or "you should get ligher work"—is fruitless. It would be better if the advisor went to the patient's plant, surveyed the conditions of work and discussed the problem with the employer. That would be an active step on the part of the medical profession towards implementing geriatrics in industry. At the present time this implementation is charged to only a handful of doctors.

It is also obvious that in certain areas neither management nor labor extend themselves sufficiently to solve the problem of the older worker. Then, too, the decisions of the Industrial Accident Commission are often unwitting barriers to the progress of the geriatric program. A meeting such as this where we are *talking to ourselves* is not the solution. It will be necessary to launch a concerted campaign designed to reach those who control the machinery involved in hiring or continuing to employ the older worker.

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# CLINICAL TRIALS WITH A NEW ANTIANEMIC AGENT—ACIDIRON

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It is common knowledge that free ionizable hydrochloric acid in the stomach is essential for the adequate utilization of ingested iron (1). The hydrochloric acid of the gastric juice ionizes the "available" iron in food and also renders the iron in solution in the acid medium (2).

The importance of hydrochloric acid is suggested by the observation in cases of chronic hypochromic anemia that the reticulocyte response is greater following the oral administration of ferric ammonium citrate in an acid medium as compared with a neutral or an alkaline medium. Gastrectomy in dogs made anemic by withdrawal of blood reduces the response to iron given orally. In discussing the role of hydrochloric acid in iron metabolism, Granick (3) states "acids, like the hydrochloric acid of the stomach, and organic acids like citrate, tartrate, lactate, etc., serve to break down ferric hydroxide and other iron compounds of the food to ferric ions or to loose ferric chelates. The ferric ions and loose ferric chelates can then be more readily reduced to ferrous ions by reducing agents of food, such as ascorbic acid, reductones, SH compounds like cysteine etc. Within recent years there has been much discussion as to whether the hydrochloric acid of the stomach plays any role in the absorption of iron, since a large number of individuals who have achlorhydria do not become deficient in iron. Consideration should, however, be given to the following facts: achlorhydria is found in adults but very rarely in growing children where the demand for iron is relatively high. Of the 20 mg. of iron ingested in the food per day in a normal diet only a small fraction, perhaps 2 mg. or less, is absorbed, and this amount of iron might be absorbed without the aid of hydrochloric acid. Organic acids in food such as citrus fruits, or the acetic acids in salads and wines, or the lactic acid in fermented milk products, may in part replace the action of hydrochloric acid and aid in bringing about the daily absorption of the 2 mg. of iron. Thus, under an adequate diet and with only a minimal iron requirement, adults may not need hydrochloric acid. However, when the iron requirement becomes relatively high the presence of hydrochloric acid may prove to be important in making more iron of the diet available for absorption, especially if the diet lacks organic acids."

Copper, manganese, cobalt, and molybdenum act as catalysts to iron absorption, but nobody has demonstrated any deficiency of these substances in human beings, and the rational use of such combinations may very well be questioned under the circumstances. As a matter of fact, Wintrobe (4) has repeatedly warned against this indiscriminate shot-gun type of therapy.

This paper describes the use of a new iron preparation, Acidiron[1], which provides ferrous sulfate coated with betaine hydrochloride, in simple oral dosage

[1] Kindly supplied by Walker Laboratories, Inc., Mount Vernon, N. Y.

form. On ingesting the tablet with a glass of water, hydrochloric acid is slowly liberated in the stomach. The hydrochloric acid acts as a catalyst to increase the rate and amount of iron absorption. Since the incidence of hypochlorhydria and achlorhydria ranges from 30 to 50 per cent in people 50 years of age and over, it was felt that the more frequent use of this combined form of therapy would be beneficial.

## METHODS

One hundred subjects ranging in age from 65 to 92 years were treated with Acidiron (Table 1), and a corresponding group was given ordinary ferrous sulfate (Table 2). A third group consisted of 66 patients ranging in age from 33 to 65 years, together with one 21-year-old woman, making a total of 67; they were treated with Acidiron (Table 3). The cases were chosen at random, with regard to sex. Only those patients were treated whose hemoglobin level was initially 10.5 Gm. per 100 cc., or lower. They received three tablets daily—one after each meal.

TABLE 1

*Treatment with Acidiron—100 subjects in age group 65–92 years*

| Primary disease | Type of anemia | Init. hemoglobin (Gm./100 cc.) | *Hemoglobin after treatment* (Gm./100 cc .) | | | | | | No. of Cases |
|---|---|---|---|---|---|---|---|---|---|
| | | | 1 wk. | 2 wks. | 3 wks. | 4 wks. | 5 wks. | 6 wks. | |
| Bleeding hemorrhoids | Hypochromic | 9.3 | 9.8 | 10.0 | 11.6 | 12.8 | 14.0 | 14.2 | 1 |
| Generalized arteriosclerosis | Normochromic | 8.2<br>9.5 | 8.8 | 9.0 | 9.2 | 9.8 | 10.1 | 11.2 | 78 |
| Chronic cervicitis | Hypochromic | 9.2<br>10.5 | 10.3 | 10.8 | 11.3 | 12.4 | 13.5 | 13.9 | 10 |
| Chronic glomerulonephritis | Normochromic | 9.0<br>10.3 | 9.6 | 9.8 | 9.8 | 9.8 | 10.0 | 10.6 | 5 |
| Undiagnosed | Hypochromic | 8.4<br>10.6 | 11.2 | 11.8 | 13.0 | 13.8 | 13.8 | 13.8 | 6 |

TABLE 2

*Treatment with Ferrous Sulfate—101 subjects in age group 65–90 years*

| Primary disease | Type of anemia | Init. hemoglobin (Gm./100 cc.) | *Hemoglobin after treatment* (Gm./100 cc.) | | | | | | No. of Cases |
|---|---|---|---|---|---|---|---|---|---|
| | | | 1 wk. | 2 wks. | 3 wks. | 4 wks. | 5 wks. | 6 wks. | |
| Generalized arteriosclerosis | Normocytic, normochromic | 9.2<br>9.5 | 9.2 | 9.4 | 9.4 | 9.6 | 9.6 | 9.6 | 89 |
| Chronic cervicitis | Hypochromic, microcytic | 9.3<br>10.0 | 9.3 | 9.3 | 9.6 | 9.8 | 9.8 | 9.8 | 9 |
| Undiagnosed | Hypochromic | 8.2<br>9.6 | 8.5 | 8.8 | 8.6 | 8.8 | 9.2 | 9.8 | 3 |

TABLE 3

*Treatment with Acidiron—67 patients in age group 33–65 years*

| Type of Anemia | Init. hemoglobin (Gm./100 cc.) | *Hemoglobin after treatment* (Gm./100 cc.) | | | No. of Cases |
|---|---|---|---|---|---|
| | | 1 wk. | 2 wks. | 3 wks. | |
| Idiopathic hypochromic | 9.7 | 10.6 | 14.2 | 14.2 | 43 |
| Nutritional achlorhydria | 8.6 | 11.1 | 13.8 | 14.6 | 2 |
| Hypochromic associated with infection | 9.4 | 10.2 | 14.0 | 14.8 | 20 |
| Pregnancy | 10.2 | 12.4 | 13.8 | 14.6 | 2 |

Each tablet of Acidiron contained 300 mg. of ferrous fulfate and the acid equivalent of 125 mg. of dilute hydrochloric acid. It must be emphasized that this is an insufficient amount of hydrochloric acid to overcome an absolute achlorhydria, but it is sufficient to act as a catalyst for absorption of iron.

## RESULTS

It is a well-known fact that anemias which occur in association with arteriosclerosis or chronic glomerulo-nephritis are resistant to anti-anemic therapy.

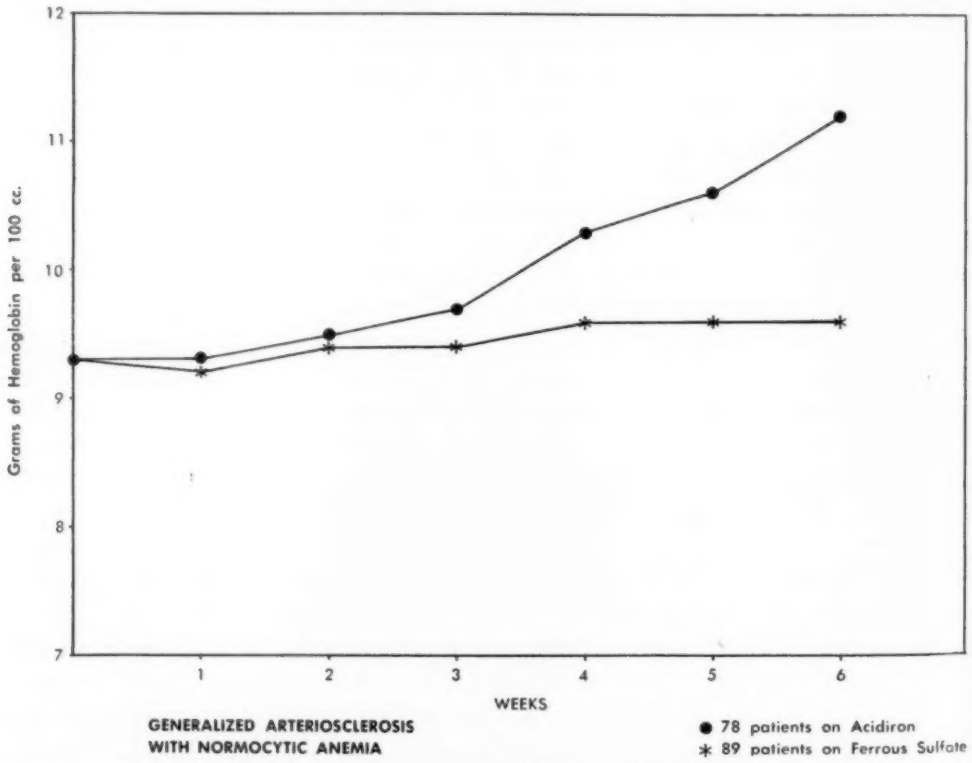


FIG. 1. Subjects aged 65–92, with generalized arteriosclerosis and normocytic anemia. Elevation of the hemoglobin level following administration of Acidiron, and practically no effect with plain ferrous sulfate.

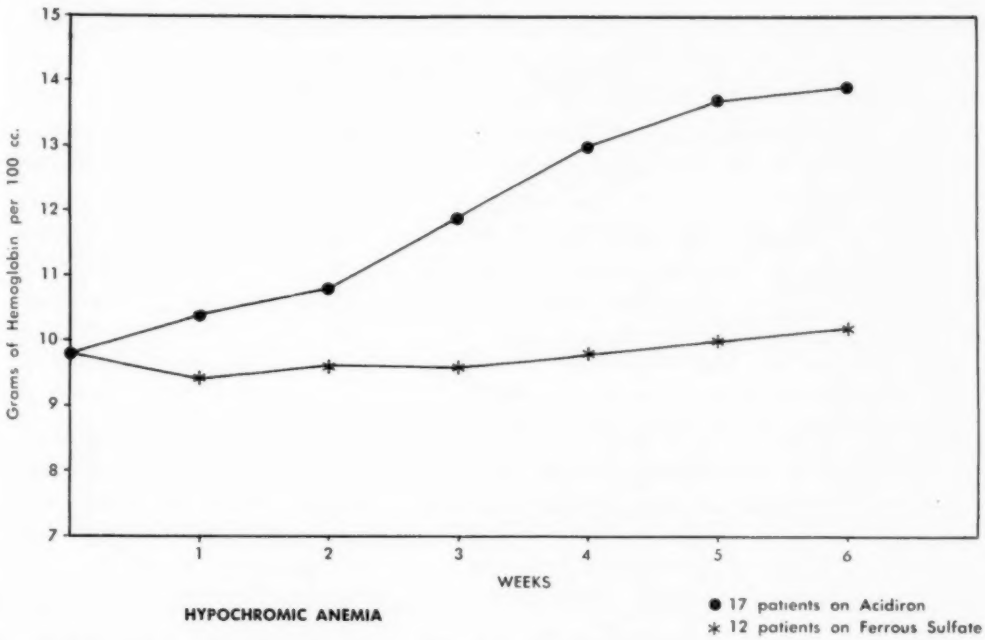


FIG. 2. Subjects aged 65–92, with hypochromic anemia. There was an elevation of about 4 Gm. per 100 cc. in the level of hemoglobin following administration of Acidiron, compared with practically no effect from plain ferrous sulfate.

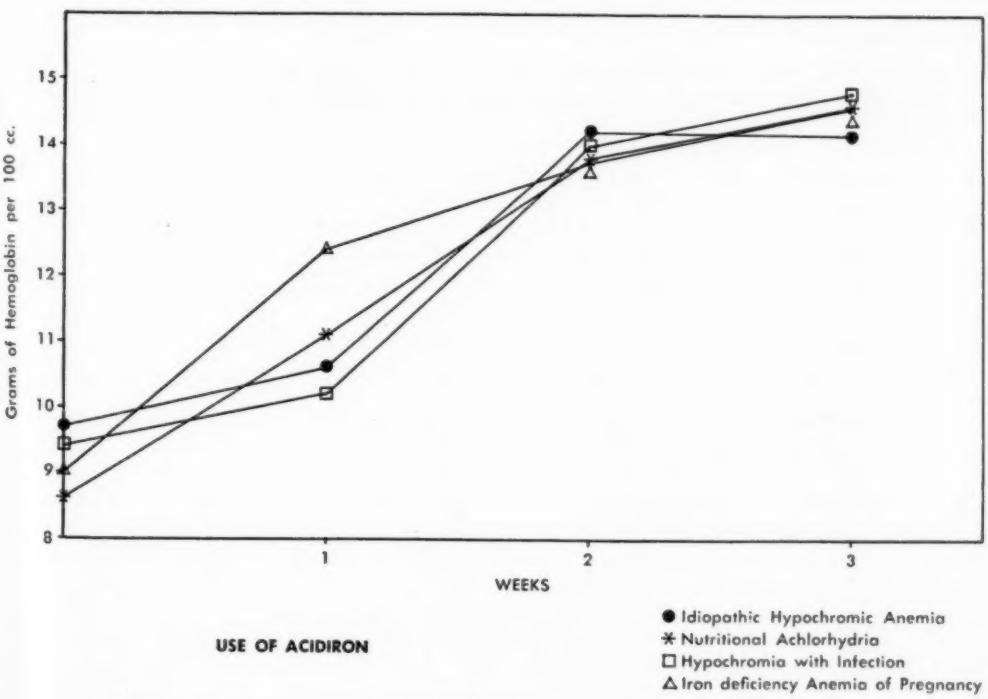


FIG. 3. Young people. Effect of Acidiron in various types of anemia.

However, Figure 1 shows clearly that there is a marked improvement when hydrochloric acid is used as a simple adjunct to iron preparations. Figure 2 shows the greater efficacy of Acidiron in hypochromic anemia of the aged. In young people, on the other hand, almost any iron preparation will suffice, including Acidiron (Fig. 3). It is felt that hydrochloric acid is not playing a role in these cases.

*Tolerance.* Of the 167 patients given Acidiron, 157 (94 per cent) reported perfect tolerance; there were minor complaints from 10 patients, whose symptoms disappeared quickly when the dosage was reduced to two tablets daily. No patient had to discontinue treatment.

## SUMMARY

An old concept of the use of hydrochloric acid along with iron therapy is again presented. A sufficient number of case studies bear out the need for more frequent use of hydrochloric acid as an adjunct to iron therapy in elderly individuals. Acidiron is specially designed to stimulate the gastric mucosa with hydrochloric acid before the ferrous sulfate is made available to the stomach. It appears from the clinical evidence submitted that hydrochloric acid, when liberated as described, activates the stomach to a physiologic state which is conducive to a more efficient systemic utilization of iron.

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# Abstracts of Current Literature

EFFECTS OF LARGACTIL IN MENTAL SYNDROMES.

Azina, H., and Ogle, W. *Canad. M. A. J.* **71:** 116 (Aug.) 1954.

One hundred patients with mental syndromes were treated for approximately three weeks with average daily doses of 400 mg. of Largactil (a phenothiazine derivative). In 74 per cent of the neurotic anxiety states, marked or moderate improvement occurred. The anxiety state usually returned upon omission of the drug. A favorable response occurred in drug addiction but not in obsessive-compulsive or mixed borderline psychoneuroses. A moderate reduction of symptoms occurred in excited, impulsive, tense, and anxious schizophrenics but not in nonexcited patients. Three patients with mania recovered, 2 remained partially refractory. Five patients with agitated depression and 3 of 15 patients with tense and anxious depression improved moderately while Largactil was continued. One patient with a hypomaniacal state in senile dementia recovered. Movements were reduced in 1 case of Huntington's chorea. Complications were maculopapular rash in 5 patients, a Parkinson-like syndrome in 4, and toxic hepatitis in 8. Jaundice appeared concomitantly with a mild epidemic of hepatitis.

INTRAVENOUS PROCAINE AMIDE AS AN AID TO DIFFERENTIATE AURICULAR FLUTTER WITH BUNDLE BRANCH BLOCK FROM PAROXYSMAL VENTRICULAR TACHYCARDIA.

Bernstein, L. M.; Pascale, L. R.; Schoolman, H. M., and Foley, E. F. *Am. Heart J.* **48:** 82 (July) 1954.

In each of 5 patients the diagnosis of auricular flutter with bundle branch block and the exclusion of paroxysmal ventricular tachycardia was accomplished by the changes resulting from intravenous administration of procaine amide. These included 1) transient decrease of atrioventricular conduction from 2:1 to 4:1, 2) decreased atrioventricular conduction, revealing flutter waves in the increased SQ segments, 3) a slightly irregular ventricular rhythm with 2° atrioventricular block changing to a more rapid regular rhythm as auricular slowing and 1:1 atrioventricular conduction occurred, and 4) change in F-R intervals so that F waves became discernible between QRS complexes. Appropriate digitalis therapy could be given in each case and its administration was avoided in wide QRS complex tachycardias in which a paroxysmal ventricular mechanism could not be excluded.

PREVALENCE OF MANIFEST ATHEROSCLEROSIS IN A WORKING POPULATION.

Boas, E. P., and Epstein, F. H. *A. M. A. Arch. Int. Med.* **94:** 94 (July) 1954.

In a random sample of working men and women aged 40 and over selected from trade union members, and examined, atherosclerosis was present in 33 per cent of the 343 men and in 23 per cent of the 225 women. The mean age of the men was 59.8 years and of the women 54 years. Four fifths of the former and two thirds of the latter were over 50 years of age. The sites of the atherosclerotic lesions were distributed as follows (expressed in percentages of the total numbers of men and women): coronary—men 10, women 2; peripheral artery—men 4, women 1; cerebrovascular—men 0.6, women 0.4. Roentgenographic evidence of aortic calcification was present in 26 per cent of the men and in 23 per cent of the women. Calcifications in the abdominal aorta were predominant in each group. Twenty-five per cent of the men and 37 per cent of the women had hypertension and in them atherosclerosis seemed to be more prevalent. Half of the cases of aortic calcification were unassociated with hypertension. Diabetes was present in 5 per cent of the men and in 8 per cent

of the women and associated with evidence of atherosclerosis in about half of each group. Although 41 per cent of the men and 54 per cent of the women were overweight, analysis of the data did not substantiate a relationship between obesity and atherosclerosis.

THE ABSORPTION OF VITAMINS AND ENZYMIC ACTIVITIES IN AGING, *in* Symposium on Problems of Gerontology, Meeting of National Vitamin Foundation and Johns Hopkins University School of Hygiene and Public Health, New York, March 1954.

Chow, B. F. (Abstr.) *Internat. Rec. Med. & Gen. Pract. Clin.* **167:** 429 (July) 1954.

The use of an oral tolerance test for determining the absorption and utilization of vitamin $B_{12}$ is described. The normal blood level of vitamin $B_{12}$ in young individuals was approximately 250 mcg. There was a 90 per cent response to 1 mg. of vitamin $B_{12}$ orally in 10 of 11 young individuals. In persons of an average age of 70 years, there was only a 40 per cent response in 14 of 36 subjects after a similar dose. Old people have a lowered vitamin $B_{12}$ binding capacity (perhaps because of a lessened amount of intrinsic factor available), which is reflected by an increased tendency toward achlorhydria. The fact that when vitamin $B_{12}$ is injected in old individuals, more of it is retained than in the young, is interpreted to mean a lesser degree of tissue saturation.

THE ARTERITIS OF RHEUMATOID ARTHRITIS.

Cruickshank, B. *Ann. Rheumat. Dis.* **13:** 136 (June) 1954.

Vascular lesions were sought in the heart and in other organs and tissues in 72 fatal cases of rheumatoid arthritis. Arteritis, past or present, was encountered in 18 cases. In 7 of these, lesions diagnostic of rheumatic heart disease were also found and the vascular involvement was mainly confined to the heart. In the remaining 11 cases, there were no pathologic processes other than rheumatoid arthritis which might be associated with the arteritis, and the vascular lesions were considered to be the arteritis of rheumatoid arthritis. The arteritis of rheumatoid arthritis was encountered most frequently in the heart, muscles, and nerves, and occasionally in synovial tissue. No vascular lesions were encountered in those viscera which are commonly affected in other forms of generalized arteritis, though diseased vessels were sometimes found in certain unusual situations, *e.g.* periosteum, oesophagus, or trachea. The arteritis usually seemed to be of subacute form, sometimes with necrosis, and it affected small arteries or arterioles. Thrombosis was unusual and aneurysm formation was not seen. Individual patients sometimes showed arterial lesions in different stages of development. The pathogenesis of the arteritis remains obscure. The vascular lesions were never regularly associated with any other lesion. The arteritis of rheumatoid arthritis, though not specifically identifiable, can be differentiated from that of polyarteritis nodosa, rheumatic fever, systemic lupus erythematosus, temporal arteritis, dermatomyositis, and scleroderma. The relation of arteritis of coronary vessels to the incidence of rheumatic heart disease in rheumatoid arthritis is discussed. The incidence of arteritis in rheumatoid arthritis is probably considerably higher than that recorded in this study. (Author's summary.)

BANTHINE AS A UROLOGIC DRUG: A CLINICAL AND ELECTROMYOGRAPHIC STUDY.

Detar, J. H.; Graham, S. D., and Corey, E. L. *J. Urol.* **72:** 45 (July) 1954.

In 7 patients with small and irritable bladders who had no evidence of genito-urinary disease, but complained of urinary frequency, Banthine increased bladder capacity, reduced intravesical pressure, and relieved frequency and nocturia. An initial intravenous injection of 100 mg. of Banthine demonstrated the effect of the drug on the bladder. Thereafter, patients received 50 to 100 mg. four times daily, depending upon response. Banthine also proved helpful in the management of spastic neurogenic bladders secondary to disease in the central nervous system. It relieved spasm in pre- and postoperative patients with

inlying catheters, and increased the capacity of small bladders during transurethral resection. The drug is contraindicated in the presence of glaucoma and in patients with lower urinary tract obstruction. Pro-Banthine has an identical action and fewer side effects.

THE INFLUENCE OF A RAPID INFUSION OF GLUCOSE ON RENAL DYNAMICS AND SODIUM EXCRETION IN PATIENTS WITH ARTERIAL HYPERTENSION.

Ek, J.; Bucht, H., and Werkö, L. *Am. Heart J.* **48:** 102 (July) 1954.

The renal clearances for inulin, endogenous creatine, sodium para-aminohippurate and sodium excretion were determined in 9 cases of arterial hypertension before and during a rapid infusion of 5 or 3 per cent glucose in water. The low basal clearances immediately increased to normal or near normal values in all cases when the rapid infusion was started. The excretion of sodium and water slowly increased during the experiment. The diuresis increased approximately to a rate about 50 per cent of the infusion rate. The sodium excretion increased up to several hundred per cent. There was a statistically significant negative correlation between the basal value for sodium excretion and the maximal value reached during the infusion. The glomerular filtration rate and sodium excretion varied independently of each other. In 4 cases in which the blood pressure was followed during and after the study, it decreased markedly for several days. (Authors' summary.)

ISCHAEMIC LATERAL POPLITEAL NERVE PALSY.

Ferguson, F. R., and Liversedge, L. A. *Brit. M. J.* **2:** 333 (Aug. 7) 1954.

Nine cases are described in which a local vascular abnormality, either thrombosis or embolism of the femoral or popliteal arteries, was followed by foot-drop. Attention is drawn to the vulnerability of the lateral popliteal nerve to ischaemia and to the underlying anatomical factors which may account for this. Clinically the local condition is shown to be relatively benign and has a good functional prognosis. (Authors' summary.)

THE CARDIAC CAN WORK.

Franko, S. C. *Indust. Med.* **23:** 315 (July) 1954.

The increasing number of older workers who have heart disease poses a serious problem to industry, because they become affected in their most productive years when their skill and experience are of greatest value. The problem can be met by adequate medical service in industry and by selective placement. Physical restrictions should be applied to the employee on the basis of his particular physical condition. The experience of Consolidated Edison Company shows that the cardiac can work. The incidence of cardiac disease among 24,473 employees in 1952 was 3.6 per cent. Among the 896 individuals affected, heart disease of the following types was present; arteriosclerotic 58.9 per cent, hypertensive vascular 32.5 per cent, rheumatic 7.2 per cent, and miscellaneous 1.4 per cent. Twenty-eight per cent of these employees were able to occupy full-time positions without physical restrictions (135 were physical workers). The remaining 72 per cent were on limited duty (172 physical workers). Almost 400 job classifications were covered. More than half of the group of 896 worked the entire year without absence due to illness. Sixty-six patients had an acute coronary thrombosis. Contrary to widespread belief as to inevitable death or permanent disability as a consequence of cardiac disease, only 22 per cent died and 7 per cent were retired for disability. Forty-six, or 69 per cent, were able to return to work after an average duration of absence of 87.2 days. One fourth of these assumed unrestricted duty. The best prognostic guides following coronary artery occlusion are the symptoms of angina and dyspnea rather than the size of the heart, the electrocardiogram, or the ballistocardiogram. Emphasis is placed on the vital role of the medical profession in the utilization by management and labor of employees with cardiac disability, and in determining the relationship of heart conditions to industrial accidents in compensation cases.

CHRONIC BARBITURATE INTOXICATION. FURTHER STUDIES.

Graser, H. F.; Isbell, H.; Eisenman, A. J.; Winkler, A., and Pescor, F. T. *A. M. A. Arch. Int. Med.* **94:** 34 (*July*) *1954.*

Fourteen men in good general health but who were addicted to barbiturates received secobarbital orally in a dose sufficiently large (0.9 to 3.8 Gm. daily) to maintain moderate to severe intoxication for thirty-two to forty-eight days. The drug was then withdrawn abruptly. The clinical manifestations of chronic barbiturism resembled those of chronic alcoholism. After abrupt withdrawal an abstinence syndrome developed, characterized by disappearance of the signs of intoxication, weakness, tremor, great anxiety, anorexia, nausea and vomiting, rapid loss of weight, fever, difficulty in making cardiovascular adjustments on standing, and convulsions of a grand mal type, with or without psychosis, which resembled alcoholic delirium tremens. Severe impairment of coordination was apparent during intoxication. Electroencephalograms were abnormal in 98 per cent of the subjects. On the second day of abstinence, a tendency to normality appeared. However, high voltage paroxysmal discharges appeared suddenly in 40 per cent of the group. This activity decreased between the fourth and eighth day and by the ninth day the patterns in 72 per cent were judged normal. Determinations were made of whole blood and serum nonprotein nitrogen and urea, serum uric acid, creatine, and creatinine levels. Creatine and creatinine values were unaltered during the addiction cycle. The other constituents were unaffected by intoxication. Following grand mal seizures in the withdrawal period, serum uric acid concentration rose sharply, was accompanied by a rise in the eosinophil count, and followed by a rise in nonprotein nitrogen. Other subjects showed similar changes of less degree. The eosinophil count returned rapidly to normal. On the basis of studies on electrically induced convulsions, the changes in uric acid and nonprotein nitrogen levels were concluded not to be specific to withdrawal of barbiturates.

BARBITURATE ADDICTION SIMULATING SPONTANEOUS HYPERSINSULINISM.

Hunter, R. A., and Greenberg, H. P. *Lancet*: **2** 58 (July 10) 1954.

Attention is drawn to the widespread use and abuse of barbiturates and the resultant problems of addiction. Three cases are reported in which a combination of irregular barbiturate dosage, dietary variations, and intoxication and abstinence symptoms produced a clinical picture resembling spontaneous hyperinsulinism. Extensive investigations gave negative results and it was only later discovered that these patients were in fact barbiturate addicts. The phenomena of chronic intoxication and withdrawal are discussed in their clinical, biochemical, and electro-encephalographic aspects, and in their relation to the frequency of barbiturate suicide. (Authors' summary.)

RELIEF OF PROSTATIC OBSTRUCTION IN THE OCTOGENARIAN.

Jacobs, A. *Lancet* **2:** 67 (July 10) 1954.

Advanced age need not be a deterrent to the removal of a prostatic obstruction. During a five-year period, prostatic obstruction was relieved by operation in 625 patients, 281 (45 per cent) of whom were aged 70 years or more and 45 (7 per cent) aged 80 years or older. The choice of technic is governed by the type of gland causing the obstruction. If it is adenomatous, retropubic prostatectomy is the preferred procedure. Nineteen of 22 patients in this group had a satisfactory postoperative course. Three died of nonsurgical causes. Two patients made a good recovery following suprapubic prostatectomy. Perurethral resection with a loop electrode is performed for obstructions caused by a fibrous prostate, sclerosis of the bladder neck, or prostatic carcinoma. Open operation may be preferred when the gland is of the large adenomatous type. Eleven of 13 patients made uneventful recoveries following this method of resection, and 2 died of other causes. Suprapubic drainage was used only when removal of an obstruction was deemed too great a hazard.

STUDIES ON THE EFFECT OF PROBENECID IN GOUT.

Mason, R. M. *Ann. Rheumat. Dis.* **13:** 120 (June) 1954.

Observations are described of 7 cases of gout treated with probenecid, urinary uric acid and blood uric acid estimations being carried out at the same time. Attacks of acute gout were studied; these occurred at a time when the level of circulating urate had been brought to normal. Attention is drawn to a possible explanation of this phenomenon: that not uric acid *per se* but a precursor may be the cause of the acute paroxysm. The use of a uricosuric agent, such as Probenecid, has enabled quantitative studies to be made which provide some evidence that uric acid in the solid phase is in equilibrium with uric acid in body fluids. (Author's summary.)

REGURGITANT ESOPHAGITIS.

McHardy, G. *Am. Pract. & Digest Treat.* **5:** 630 (Aug.) 1954.

Comparison of the original diagnoses with those rendered after careful analysis of 100 patients with unsatisfactory response of anterior chest pain to previous medical care, indicates that the tendency to consider chest pain synonymous with cardiovascular disease is erroneous. The importance of regurgitant esophagitis as a clinical entity is presented in relation to the complaint of supradiaphragmatic pain. McHardy concludes that the etiology of this occurrence is probably mechanical incompetency of the esophagogastric junction, with some inconstant and poorly understood related factors. Diagnostic studies should be made, and the true severity of the disease established prior to electing a therapeutic program. Medical trial should probably precede surgery in all instances other than those with severe complications. Complications and severity may necessitate operation. The responsibility of such election must be accepted with appreciation of consequent complications, morbidity and recurrence.

A RARE PRESENILE DEMENTIA ASSOCIATED WITH CORTICAL BLINDNESS (HEIDENHAIN'S SYNDROME).

Meyer, A.; Leigh, D., and Bagg, C. E. *J. Neurol., Neurosurg. & Psychiat* **17:** 129 (May) 1954.

A rare condition is described, for which the name Heidenhain's syndrome is proposed. It was characterized by a rapid course, cortical blindness, and dementia. Pathologically there was diffuse cortical degeneration particularly of the occipital cortex, in which there was a spongiose state. The condition resembled that previously described by Heidenhain and classified as belonging to the Creutzfeld-Jakob syndrome. However, because of the rapid clinical course, cortical changes primarily in the occipital lobe instead of in the motor cortex, and with no prominent affection of the basal ganglia, the case reported and 2 reported by Heidenhain form a distinct group. The rarity of the condition will probably preclude an accurate diagnosis.

SIGMOIDOSCOPY: PROCEDURE OF CHOICE FOR DETECTION OF PRE-MALIGNANT. LESIONS OF THE COLON AND RECTUM.

Miller, D. *Am. Pract. & Digest Treat.* **5:** 640 (Aug.) 1954.

The sigmoidoscope is the instrument of choice in the detection of lesions within the distal 25 cm. of the gut. Above this level, insertion of the sigmoidoscope through any openings furnishes important information concerning the state of the colonic mucosa. Sigmoidoscopy is mastered easily with practice. Provided the sigmoidoscope is advanced gently under visual guidance and the examination is discontinued if the opening ahead is obscured by stool or impassable lesions, the procedure involves little hazard. (Author's conclusions.) Sigmoidoscopy, it is believed, should have an important place in general physical examinations of persons in the fourth decade and beyond.

OBSTRUCTIVE ARTERIAL DISEASE IN THE AGED.
Naide, M. *Pennsylvania M. J.* **57:** 742 (Aug.) 1954.

Occlusion may result from arteriosclerosis obliterans. The diagnosis is made from the history and physical examination. An ischemic foot blanches rapidly on elevation, on dependency has a delayed flushing time, and is cooler than a foot with normal circulation. X-ray examination shows arterial calcification. A vasodilatation test or posterior tibial nerve block shows the degree of collateral circulation. In acute arterial occlusion, embolism and thrombosis must be differentiated, as embolectomy in early cases may be limb-saving when ischemia is extreme. Embolism is the probable diagnosis whenever there is a likely source. Anticoagulants are indicated in both. In elderly patients especially, severe peripheral arterial occlusion must be distinguished from neurologic conditions such as cerebral arterial occlusion. When an extremity has no pulses and is cold, peripheral arterial occlusion is the diagnosis rather than a cerebrovascular incident. Treatment attempts to prevent trauma to ischemic tissue and to maintain the patency of collateral vessels. Blood flow is increased by physical (heat, elevation of the head), medical (vasodilators, intra-arterial papaverine), and surgical methods (sympathetic ganglion or sciatic block, caudal anesthesia, avoiding a drop in blood pressure in the elderly). Lumbar sympathectomy increases blood flow to the skin but is contraindicated if gangrene is extensive. Walking distance in intermittent claudication may be increased by teaching slow progression. Bed rest and antibiotics are essential in the treatment of lesions. Physiologic saline soaks are used for a few days at a time. Toe amputation is feasible in some patients and transmetatarsal amputation in others. Present rehabilitation methods permit older individuals to use prosthetic devices successfully.

INTRAVENOUS PROCAINE AMIDE IN THE TREATMENT OF CARDIAC ARRHYTHMIAS.
Pascale, L. R.; Bernstein, L. M.; Schoolman, H. M., and Foley, E. F. *Am. Heart J.* **48:** 110 (July) 1954.

Procaine amide intravenously converted 10 of 13 episodes of supraventricular tachycardia to sinus rhythm. In 7 instances 500 mg. or less were required and in 3 instances 800 to 1,400 mg. In 3 patients failure to convert was due to hypotension. If hypotension occurs when procaine amide is the first agent used in treatment, its administration should be interrupted. If the tachycardia has failed to convert with other medications, then the hypotension should be corrected with *l*-norepinephrine before proceeding with procaine amide treatment. None of 8 episodes of auricular flutter treated were converted. Episodes of intermittent paroxysmal ventricular tachycardia in 3 patients were suppressed with 400 mg. or less of procaine amide. Seventeen episodes of persistent paroxysmal ventricular tachycardia in 13 patients were suppressed with doses of 300 to 2,500 mg. All except 1 of these patients had organic heart disease and in 9 an acute myocardial infarction was demonstrated by postconversion electrocardiograms. Hypotension was controlled with *l*-norepinephrine. Widening of the QRS complexes was noted in the patients treated. Convulsions and death followed procaine amide therapy in 1 instance.

SPECIAL NUTRITIONAL PROBLEMS OF THE AGED, *in* Symposium on Problems of Gerontology, Meeting of National Vitamin Foundation and Johns Hopkins University School of Hygiene and Public Health, New York, March 1954.
Rafsky, H. A. (Abstr.) *Internat. Rec. Med. & Gen. Pract. Clin.* **167:** 439 (July) 1954.

Low serum carotene and vitamin A levels are present in a significant number of elderly subjects. Impaired utilization rather than impaired or reduced absorption of vitamin A was found. Protein deficiency is often seen. Studies revealed the total plasma protein content near normal in elderly individuals, but a significant decrease in concentration of al-

bumin and an increase in the globulin fraction, particularly of the beta-globulin fraction, were found. Hepatic dysfunction occurs in 80 to 90 per cent of aged individuals. The use of crude liver extract seemed to improve significantly the symptoms of fatigue in many elderly individuals and it was more effective than B-complex vitamins alone. The absorption and tissue saturation of vitamin $B_{12}$ were much lower in the aged than in young individuals.

EARLY DIAGNOSIS OF PROSTATIC CARCINOMA.

Reese, L. *Canad. M. A. J.* **71:** 149 (Aug.) 1954.

Carcinoma cells can be found in prostatic secretion, and finding them justifies the diagnosis of cancer of the prostate. The presence of cancer cells, and in the case of the more differentiated cancers, the presence of clusters of cancer cells, is essential for the diagnosis of prostatic cancer. Cancer cells were detected in cases in which the diagnosis could not be made on the basis of rectal examination. A smear, therefore, is of value as a screening test. Its greatest virtue is that it permits recognition of malignancy at a relatively early stage, and in instances in which other diagnostic methods may fail. It is feasible to use it as an adjunct to diagnosis and as a screening test for carcinoma of the prostate. (Author's summary.)

DETECTION OF EARLY PROSTATIC AND URINARY TRACT CANCER IN ASYMPTOMATIC PATIENTS FIFTY YEARS OF AGE AND OVER.

Riaboff, P. J. *J. Urol.* **72:** 62(July) 1954.

A preliminary report is presented on the cytologic study of the prostatic secretion and urine sediment from 1,738 asymptomatic male patients 50 years of age and over. These patients were examined at the Strang Prevention Clinic, Memorial Center, during a period of three years. Clinically suspicious cases were excluded from this study. Two proven cases, an unsuspected grade I carcinoma of the bladder and a clinically unsuspected adenocarcinoma of the prostate, were detected primarily by the cytologic method. The cytologically suspicious and atypical cases in this group of patients have not been confirmed clinically or pathologically. The difficulty involved in proving the presence of a prostatic carcinoma based upon suspicious or positive cytologic findings without clinical evidence necessitates a long-term follow-up of these patients, with careful clinical evaluation and repeated cytologic studies. Further knowledge concerning the identification and significance of many of the unknown cells appearing in the prostatic secretion and in the urine after massage is now in the process of being obtained by restudy and re-evaluation of smears, as well as the study of tissue sections from the various areas of the genito-urinary tract. At the present time it can only be concluded that this project must be continued on a research basis for a number of years before its value can be accurately estimated in cancer detection clinics or in the physician's office. (Author's summary and conclusions.)

*d*-AMPHETAMINE THERAPY IN OBESITY OR DEPRESSION COMPLICATED BY BENIGN HYPERTENSION.

Roberts, E. *Am. Pract. & Digest Treat.* **5:** 606 (Aug.) 1954.

From a study of the pressor activity of *d*-amphetamine sulfate in 76 obese, or obese and depressed patients with benign hypertension, it is concluded that the drug in daily doses of 10 to 15 mg. is not contraindicated in the latter condition. Pressor effects were slight or absent in both ambulatory and bed patients, 56 of whom were between the ages of 50 and 89 years.

CARCINOMA OF THE SEMINAL VESICAL: REPORT OF TWO CASES.
Smith, B. A., Jr. *J. Urol.* **72:** 67 (July) 1954.

Two cases of primary carcinoma of the seminal vesicles have been described in detail, bringing the reported cases to 28; at least 4 other cases have been observed. It is believed that the lesion should be recognized clinically and may be proved by biopsy, cystoscopic if feasible, or perineal if the lesion is early, in which event local excision may be possible. Prostatovesiculocystectomy would seem to be the logical and most thorough therapy from the standpoint of attempted cure. The insoluble sulfonamides seem to be contraindicated in anticipated ureterointestinal anastomosis. (Author's summary.)

# AMERICAN GERIATRICS SOCIETY

# THE 1955 ANNUAL MEETING

The 12th Annual Meeting of the American Geriatrics Society will be held at the *Hotel Roosevelt* in *New York City* on *April 21 and 22, 1955.*

The Hotel Roosevelt in New York has set aside a number of rooms to take care of Fellows who plan to attend the meeting. Write to Mr. A. G. Schellenberg, Reservation Manager, Hotel Roosevelt, Madison Avenue at 45th Street, New York 17, N. Y. Mention that you will attend the annual meeting and Mr. Schellenberg will be glad to take care of your needs.

The Scientific Sessions will be held in the Palm Terrace Room.

The Annual Business Meeting will be held in the Palm Terrace Room immediately following the close of the afternoon session on Thursday, April 21.

The Annual Dinner is scheduled for the Palm Terrace Room on Friday evening, April 22, at 8 o'clock preceded by cocktails in the foyer of the Palm Terrace Room at 7 o'clock.

Dr. Thomas H. McGavack, Flower and Fifth Avenue Hospitals, New York, is the Chairman of the Local Arrangements Committee—Drs. Edward B. Allen, Harry A. Coveler, C. Ward Crampton, Cortez Enloe, Cornelius P. Rhoads, Harry Seneca.

Norris J. Heckel, M.D.
*President*

## SCIENTIFIC PROGRAM

### HOTEL ROOSEVELT

### MORNING SESSION—THURSDAY, APRIL 21

*Norris J. Heckel, M.D.*, presiding

8:00 Registration

9:00 Dermatologic Problems in the Aged
*Morris Leider, M.D., New York, N. Y.*

9:15 Problems Peculiar to Surgery in the Aged—An Analysis of Over 300 Surgical Operations
*Arkell M. Vaughn, M.D. and Michael S. White, M.D., Chicago, Illinois*

9:30 Diagnosis and Therapy of Migraine
*Harold W. Lovell, M.D., New York, N. Y.*

9:45 Results of Treatment of Fractures of the Neck of the Femur in the Aged
*M. S. Goldstein, M.D., C. L. Beye, M.D., M. Bonfiglio, M.D. and S. E. Ziffren, M.D., Iowa City, Iowa*

10:00–10:20 Question Period
10:20–10:30 Recess for Refreshments

*Edward Henderson, M.D.*, presiding

10:30 MANAGEMENT OF BLADDER DYSFUNCTIONS IN THE PARAPLEGIC PATIENT
*John Kingsley Lattimer, M.D., New York, N. Y.*

10:45 RECENT DEVELOPMENTS IN THE THERAPY OF CHRONIC RESPIRATORY DISEASES
*Carl Muschenheim, M.D., New York, N. Y.*

Question Period—*Malford W. Thewlis, M.D.*, presiding

11:00–12:45 **PANEL ON DIABETES IN THE AGED**

Moderator:
*Laurance W. Kinsell, M.D., Oakland, California*
Collaborators:
*Howard Root, M.D., Boston, Mass.*
*Thomas H. McGavack, M.D., New York, N. Y.*
*Irving Graef, M.D., New York, N. Y.*
*Herbert Pollack, M.D., New York, N. Y.*
*Beverly C. Smith, M.D., New York, N. Y.*
*Edward Tolstoi, M.D., New York, N. Y.*

12:45 LUNCHEON

**AFTERNOON SESSION—THURSDAY, APRIL 21**

*Richard J. Kraemer, M.D.*, presiding

1:45 CAUSES AND MANAGEMENT OF POSTMENOPAUSAL UTERINE BLEEDING
*J. Donald Woodruff, M.D., Baltimore, Maryland*

2:00 PELVIC FINDINGS IN WOMEN AFTER 65
*Dean Farley, M.D., and John R. Wolff, M.D., Chicago, Illinois*

2:15 CORRELATION OF X-RAY DIFFRACTION AND METAL CONTENT OF AGING AORTA
*Hans H. Zinsser, M.D., Los Angeles, California*

2:30 TUBE FEEDING IN ELDERLY PATIENTS
*James Barron, M.D. and L. S. Fallis, M.D., Detroit, Michigan*

2:45 MANAGEMENT OF ANESTHESIA IN THE OLDER AGE GROUP
*John E. Osborn, M.D., Rochester, Minnesota*

3:00–3:20 Question Period
3:20–3:30 Recess for Refreshments

*Edward B. Allen, M.D.*, presiding

3:30–5:30 **PANEL ON CARDIAC AND CIRCULATORY DISEASES**

Moderator:
*C. T. Stone, M.D., Galveston, Texas*
Collaborators:
*George Griffith, M.D., Los Angeles, California*
*Hugh Montgomery, Philadelphia, Pa.*
*Oglesby Paul, Chicago, Ill.*
*Gerald H. Pratt, New York, N. Y.*

5:30 **Business Meeting**—Limited to members only.

**MORNING SESSION—FRIDAY, APRIL 22**

*Hollis E. Clow, M.D.*, presiding

8:00 REGISTRATION

9:00 DIAGNOSIS AND TREATMENT OF CHRONIC GLAUCOMA
*William F. Hughes, Jr., M.D., Chicago, Illinois*

9:15 THE DILEMMA OF GASTRIC ULCER—BENIGN OR MALIGNANT? A PLAN OF MANAGEMENT FOR GERIATRIC PATIENTS
*Brock E. Brush, M.D. and Robert J. Priest, M.D., Detroit, Michigan*

9:30 TREATMENT OF INTESTINAL OBSTRUCTION IN THE AGED
*Frank Glenn, M.D. and George Wantz, M.D., New York, N. Y.*

9:45 CONCERNING THE DIAGNOSIS AND TREATMENT OF SUBDURAL HEMORRHAGE IN THE AGED
*Matthew T. Moore, M.D., Philadelphia, Pa.*

10:00–10:20 Question Period

10:20–10:30 Recess for Refreshments

*Thomas H. McGavack, M.D.*, presiding

10:30 JAUNDICE IN THE AGED: DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS
*Frederick Steigmann, M.D. and V. Godellas, M.D., Chicago, Illinois*

10:45 URINARY 17-KETOSTEROID EXCRETION AS INFLUENCED BY AGE AND DISEASE
*Thomas H. McGavack and Sidney Pearson, New York, N. Y.*

11:00–12:45 **PANEL ON OSTEOPOROSIS**

Moderator:
*Ephraim Shorr, M.D., New York, N. Y.*

Collaborators:
*Daniel Laszlo, M.D., New York, N. Y.*
*Nathan W. Shock, Ph.D., Baltimore, Md.*
*G. Donald Whedon, M.D., Bethesda, Md.*
*Harry L. Jaffe, M.D., New York, N. Y.*

12:45–1:45 LUNCHEON

## AFTERNOON SESSION—FRIDAY, APRIL 22

*Harold G. Wolff, M.D.*, presiding

1:45 DIAGNOSIS AND TREATMENT OF PAIN IN THE ACROMIO-CLAVICULAR JOINT
*Charles V. Heck, M.D. and Fremont A. Chandler, M.D., Chicago, Illinois*

2:00 THE PREFERENCE FOR STREPTODUOCIN IN THE TREATMENT OF TUBERCULOSIS OF THE AGING
*Harry Shubin, M.D., Philadelphia, Pa.*

2:15 ROENTGEN THERAPY IN CHRONIC CHEST SYMPTOMS IN THE ELDERLY
*Anthony F. Rossitto, M.D., Wichita, Kansas*

2:30 THE TREATMENT PARKINSON'S DISEASE IN THE AGED
*Robert S. Schwab, M.D., Boston, Mass.*

*Laurance W. Kinsell, M.D.*, presiding

2:45–4:45 **PANEL ON CANCER**

Moderator:
*C. P. Rhoads, M.D., New York, N. Y.*

Collaborators:

HORMONAL THERAPY IN CANCER
*Rulon W. Rawson, M.D., New York, N. Y.*

EVALUATION OF ADRENALECTOMY FOR CANCER OF THE PROSTATE AND BREAST
*H. T. Randall, M.D., New York, N. Y.*

PALLIATIVE THERAPY OF CANCER OF THE LUNG
*D. A. Karnofsky, M.D., New York, N. Y.*

THE INDICATIONS FOR THE USE OF ISOTOPES IN MALIGNANT DISEASES
*J. E. Rall, M.D., New York, N. Y.*

## PAPERS READ BY TITLE

TURNING BACK THE CLOCK
*Simeon C. Allen, M.D., Boston, Mass.*

CONGENITAL HEART DISEASE IN THE AGED
*Louis F. Bishop, M.D., New York, N. Y.*

ADVANTAGES OF AMBULATORY PROCTOLOGY TECHNIQUES IN THE ELDERLY PATIENT
*Alfred J. Cantor, M.D., Long Island, N. Y.*

ARTERIOSCLEROSIS AND MODERN LIVING
*Aris Carpousis, M.D., Washington, D. C.*

CARCINOMA OF THE BREAST IN THE AGED
*T. C. Case, M.D., New York, N. Y.*

EARLY DIAGNOSIS OF CHRONIC DISEASE. USE OF EMISSION SPECTROSCOPE IN DETERMINATION OF TRACE ELEMENTS IN HUMAN BLOOD
*Henry Eisfelder, M.D., Roslyn Heights, N. Y.*

THE USE OF DIGITALIS IN THE GERIATRIC PATIENT
*Samuel Epstein, M.D., Brooklyn, N. Y.*

A GERIATRIC CLINIC IN A GENERAL HOSPITAL—FIRST YEAR'S EXPERIENCE
*Louis Friedfeld, M.D., New York, N. Y.*

NEWER ASPECTS AND TECHNIQUES IN GERIATRIC PSYCHIATRY
*Hal W. Geyer, M.D., Milford, Delaware*

ATTITUDE THERAPY FOR NON-INSTITUTIONALIZED ELDERLY PSYCHOTICS
*Ralph Ginzberg, M.D., Tomah, Wisconsin*

SERUM BETA-LIPOPROTEIN IN THE AGED: METABOLIC CORRELATION
*Leo Gitman, M.D., Brooklyn, N. Y.*

SHOCK THERAPY FOR THE AGED (INDICATIONS, PROCEDURE AND RESULTS)
*Hirsch Loeb Gordon, M.D., New York, N. Y.*

THE USE OF DESOXYCORTICOSTERONE ACETATE IN THE TREATMENT OF GASTRIC AND DUODENAL ULCERS
*George Joyce Hall, M.D., Sacramento, Calif.*

MEDICAL CARE IN THE OLD AGE ASSISTANCE PROGRAM
*William Hammond, M.D., Scarsdale, N. Y.*

ARRHYTHMIAS OF THE AGED
*Raymond Harris, M.D., Albany, N. Y.*

HERNIA IN THE AGED
*A. H. Iason, M.D., Brooklyn, N. Y.*

GALLBLADDER SURGERY IN THE AGED
*C. R. Jablonoski, M.D., Cleveland, Ohio*

EFFORT, STRESS, AND CORONARY HEART DISEASE
*Edmund Jacobson, M.D., Chicago, Illinois*

SALIENT FACTORS IN BRIEF PSYCHOTHERAPY WITH PATIENTS IN LATER LIFE
*Hans J. Kleinschmidt, M.D., New York, N. Y.*

CURE OF BLINDNESS IN THE OLDER AGE GROUP
*Arthur Alexander Knapp, M.D., New York, N. Y.*

THE MEANING AND IMPORTANCE OF POTASSIUM IN PLASMA DETERMINATION DURING THE FOUR-HOUR GLUCOSE TOLERANCE TEST IN VISCEROPTOSIS WITH FUNCTIONAL HYPERINSULINISM
*H. Layzer, M.D., Cleveland, Ohio*

REAPPRAISAL OF TODAY'S NUTRITION
*W. Coda Martin, M.D., New York, N. Y.*

PSYCHOTHERAPY NEEDED IN SENESCENT MARRIED COUPLES (CASE REPORTS AND THEORETICAL SURVEY)
*Joseph Meiers, M.D., New York, N. Y.*

THE USE OF A CARBONIC ANHYDRASE INHIBITOR IN THE TREATMENT OF HYPERKALIEMIA
*Vince Moseley, M.D., Charleston, S. C.*

USE OF HYALURONIDASE IN PEYRONIE'S DISEASE
*C. L. Mulinger, M.D., Los Angeles, Calif.*

MANAGEMENT OF CATARACT
*Brittain Ford Payne, M.D., New York, N. Y.*

THE USE OF INTRACUTANEOUS AND DEPOT HISTAMINE IN THE TREATMENT OF OSTEOARTHRITIS AND FIBROSITIS
*Irving B. Perlstein, M.D., Louisville, Ky.*

SENILE MACULAR DEGENERATION OF THE EYES—WITH CASE REPORTS
*Louis F. Raymond, M.D., East Orange, N. J.*

NEURO-GERIATRICS; ORGANIC AND PHILOSOPHICAL CONCEPTS
*Karl Rothschild, M.D., New Brunswick, N. J.*

1. THE SIGNIFICANCE OF LONG-STANDING HERNIA TO THE GERIATRIC PATIENT. 2. OCCLUSIVE ARTERIAL GANGRENE IN THE OLDER PATIENT
*Martin E. Silverstein, M.D., New York, N. Y.*

PREMATURE VASCULAR DEGENERATION IN DIABETES MELLITUS—PATHOGENESIS, AND RELATION TO AGING
*Chester Solez, M.D., Narragansett, R. I.*

THE ROLE OF THE SOCIAL WORKER IN REHABILITATION IN AN INSTITUTION FOR THE CHRONICALLY ILL
*Mrs. Helen K. Weil, Cleveland Heights, Ohio*

## A SPECIAL INVITATION TO ALL FELLOWS AND MEMBERS OF THE AMERICAN GERIATRICS SOCIETY

Through the kind cooperation of Miss Frances King, Director, the William I. Sirovich Day Center, 203 Second Avenue, New York City, will be open on Saturday morning, April 23, especially to welcome our Members and Fellows to see and study the splendid work that is being done in this center. The center sponsors a cultural and educational program for older people, and although it has been in existence for a matter of only six years it has already won acclaim for its fine work.

The center has succeeded in its endeavor to offer the older men and women a substitute for such factors as the loss of a workday, loss of routine, or loss of companions.

A visit to the center is an inspiring experience and all Fellows and Members are urged to accept Miss King's kind invitation.